EVALUATION of VESTIBULAR FUNCTION

with VISUAL FEEDBACK POSTUROGRAPHY and MOTORIZED HEAD IMPULSE TEST

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MEELI HIRVONEN

Academic dissertation

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CONTENTS

ABSTRACT

Objectives: To evaluate the applicability of visual feedback posturography (VFP) for quantification of postural control, and to characterize the horizontal angular vestibulo-ocular reflex (AVOR) by use of a novel motorized head impulse test (MHIT).

Methods: In VFP, subjects standing on a platform were instructed to move their center of gravity to symmetrically placed peripheral targets as fast and accurately as possible. The active postural control movements were measured in healthy subjects (n = 23), and in patients with vestibular schwannoma (VS) before surgery (n = 49), one month (n = 17), and three months (n = 36) after surgery. In MHIT we recorded head and eye position during motorized head impulses (mean velocity of 170º/s and acceleration of 1 550º/s²) in healthy subjects (n = 22), in patients with VS before surgery (n = 38) and about four months afterwards (n = 27). The gain, asymmetry and latency in MHIT were compared with unilateral weakness in a caloric test and subjective symptoms.

Results: The intraclass correlation coefficient for VFP parameters during repeated tests was significant ($r = 0.78\text{-}0.96$; $p < 0.01$), although two of four VFP parameters improved slightly during five test sessions in controls. At least one VFP parameter was abnormal pre- and postoperatively in almost half the patients, and these abnormal preoperative VFP results correlated significantly with abnormal postoperative results. The mean accuracy in postural control in patients was reduced pre- and postoperatively. A significant side difference with VFP was evident in 10% of patients. In the MHIT, the normal gain was close to unity, the asymmetry in gain was within 10%, and the latency was a mean ± standard deviation 3.4 ± 6.3 milliseconds. Ipsilateral gain or asymmetry in gain was preoperatively abnormal in 71% of patients, whereas it was abnormal in every patient after surgery. Preoperative gain (mean ± 95% confidence interval) was significantly lowered to 0.83 ± 0.08 on the ipsilateral side compared to 0.98 ± 0.06 on the contralateral side. The ipsilateral postoperative mean gain of 0.53 ± 0.05 was significantly different from preoperative gain. Results of vestibular tests did not correlate with the symptoms of dizziness.

Conclusion: The VFP is a repeatable, quantitative method to assess active postural control within individual subjects. The mean postural control in patients with VS was disturbed before and after surgery, although not severely. Side difference in postural control in the VFP was rare. The horizontal AVOR results in healthy subjects and in patients with VS, measured with MHIT, were in agreement with published data achieved using other techniques with head impulse stimuli. Vestibular disability could not be predicted based on AVOR performance either in MHIT or in the caloric test. The MHIT is a non-invasive method which allows reliable clinical assessment of the horizontal AVOR.

ABBREVIATIONS

AVOR	angular vestibulo-ocular reflex
BI	balance index
CI	confidence interval
CMV	center of gravity marker velocity
COG	center of gravity
EOG	electro-oculography
HD	hit delay
HP	hold percentage
HTT	head thrust test
MHIT	motorized head impulse test
MSC	magnetic search coil
SCC	semicircular canal
SD	standard deviation
SV	sway velocity
VFP	visual feedback posturography
VS	vestibular schwannoma

LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following original papers, referred to in the text by the Roman numerals I-V:

I Hirvonen TP, Hirvonen M, Aalto H. Postural control measured by visual feedback posturography. ORL J.Otorhinolaryngol.Relat.Spec. 64(3):186-190, 2002.

II Hirvonen M, Aalto H, Hirvonen TP. Preoperative postural control of patients with vestibular schwannoma assessed by visual feedback posturography. ORL J.Otorhinolaryngol.Relat.Spec. 68(4):232-236, 2006.

III Hirvonen M, Aalto H, Hirvonen TP. Postural control after vestibular schwannoma resection measured with visual feedback posturography. ORL J.Otorhinolaryngol.Relat.Spec. 67(6):335-339, 2005.

IV Hirvonen M, Aalto H, Migliaccio AA, Hirvonen TP. Motorized head impulse rotator for horizontal vestibulo-ocular reflex: Normal responses. Arch.Otolaryngol.Head.Neck.Surg. 133(2):157-161, 2007.

V Hirvonen M, Aalto H, Hirvonen TP. Motorized head impulse rotator in patients with vestibular schwannoma. Acta Otolaryngol.(Stockh) 128(11):1215-1220, 2008.

1. INTRODUCTION

Vertigo and dizziness are among the most frequent complaints encountered in general clinical practice, and about 44% of these are caused by peripheral vestibular disorders (Kroenke et al. 2000). The vestibular system is responsible for maintaining balance, keeping vision stable, and assisting in controlling movements. The angular vestibulo-ocular reflex (AVOR), which connects the vestibular part of the labyrinth with the extrinsic eye muscles, keeps the vision stable on the retina while the head is turning. The vestibulospinal reflexes keep the head and body stable in space. Thus, evaluation of both vestibulo-ocular and vestibulospinal pathways is essential in balance disorders.

No single test can assess the entire vestibular labyrinth, since there are five vestibular end organs: three semicircular canals (SCCs) and two otolith organs on each side. The caloric test has been considered superior to the sinusoidal rotatory tests, as each labyrinth can be studied separately. However, thermal irrigation stimulates only the horizontal SCC, and the stimulation matches a much lower frequency than natural frequencies of head movements (0.004 Hz versus 0.7-8 Hz). The head thrust test (HTT) uses rotation in each direction separately, and it relies on Ewald's second law (Ewald 1892), which states that an excitatory response is much larger than an inhibitory. The HTT allows AVOR testing at bedside by using detection of refixation saccades as an indirect sign of SCC hypofunction. The manually delivered quantitative head impulse test, which uses a magnetic search coil (MSC) to measure eye movement, allows a precise quantification of AVOR during more natural velocities (Halmagyi et al. 1990). Because the quantitative head impulse test is invasive and demanding in a test setting, it is available in only a limited number of vestibular laboratories. Additionally, the quantitative head impulse test is variable in stimulus intensity. Tabak and Collewijn (1994) introduced helmet-driven, motorized head movements instead of manual stimuli to homogenize the intensity of the head impulse stimulus. They used the MSC technique, and their well-controlled impulses achieved accelerations and velocities which were low, making it more difficult to extract the AVOR response separately from each side. Taking all these requirements together, we constructed a more powerful, noninvasive, motorized head impulse rotator for clinical evaluation of AVOR.

Objective methods to evaluate human posture are still lacking, due to the complexity of postural control. Posturography is an objective method to quantify postural stability. Static posturography measures postural sway on a stable platform, whereas dynamic posturography uses a force platform combined with vestibular, visual, and somatosensory stimuli (Nashner 1993). Due to their low specificity in localizing vestibular lesions, both modalities of posturography have been mainly used in follow-up and monitoring of rehabilitation in patients

with balance disorders. The principle of visual feedback posturography (VFP) has been introduced as a tool to practice postural control and evaluate the results of vestibular rehabilitation (Shumway-Cook et al. 1988). As one part of this thesis, we employed a custom-made VFP, in which the subjects use their postural control actively by leaning on the platform to reach targets within different directions of the subject's stability limits.

The purpose of this study was to investigate the clinical potential (1) of VFP in assessment of posture, and (2) of the motorized head impulse rotator in assessment of horizontal AVOR, in healthy volunteers and in patients with vestibular schwannoma (VS).

2. REVIEW OF THE LITERATURE

2.1 ANATOMY OF THE PERIPHERAL VESTIBULAR SYSTEM

The peripheral part of the vestibular system consists of the labyrinth, which includes the horizontal, superior, and posterior SCCs as well as the utricle and saccule, and their projections to the brainstem. Each SCC has a synergistic canal on the opposite side lying approximately parallel to it. The horizontal canals act as a pair, while each anterior canal is paired with the posterior canal on the opposite side. The front parts of horizontal canals are tilted upwards approximately 20º, and they are inclined towards each other about 11º (Figure 1). The anteroposterior canal planes deviate by about 15º (Della Santina et al. 2005). This structure implies that rotation in any canal plane will cause some stimulation of all canals (Curthoys et al. 1977).

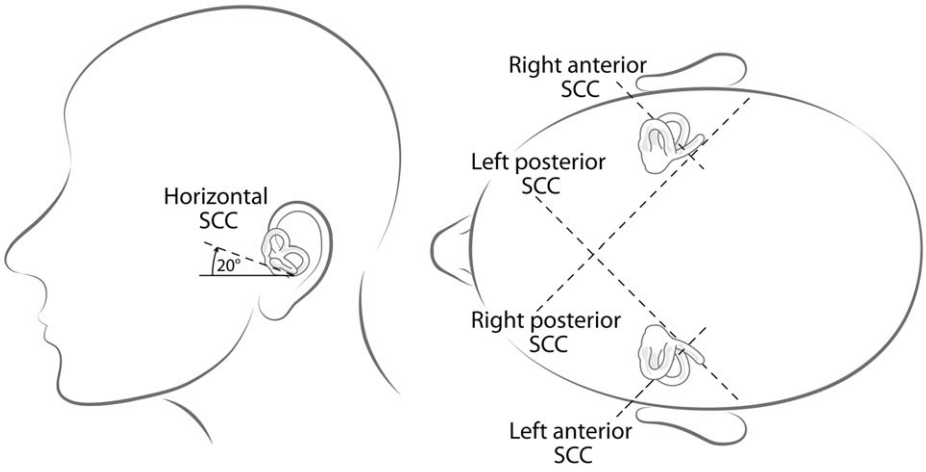

Figure 1. *Orientation of semicircular canals (SCCs). The horizontal SCC is tilted at its anterior end approximately 20º upward from the horizontal plane. The left anterior SCC is coplanar with the right posterior SCC, and vice versa.*

Membranous SCCs, arising from the vestibule, have near one end a widening known as the ampulla, which contains the crista ampullaris and cupula. The crista is a ridge of neurosensory epithelium containing hair cells. Each hair cell contains a bundle of 50 to 100 stereocilia and one kinocilia at the edge of each bundle. The hair cells have a morphologic polarization: deflection of the stereocilia toward the kinocilium produces excitation, and deflection of the stereocilia away from the kinocilium produces inhibition (Wersall 1956, Wersall et al. 1965). The hair cells are oriented in the horizontal SCC in such a way that endolymph flow towards the ampulla (ampullopetal) results in excitation of hair cells, whereas flow away from the ampulla (ampullofugal) leads to inhibition (Figure 2). When the angular acceleration occurs in a particular plane, the coplanar canals from each labyrinth are stimulated in opposite directions, producing simultaneously excitation in one and inhibition in the other canal (Gacek 2005). The utricle and saccule, together called the otolith organs, contain hair cells covered by macula. One macula is attached horizontally to the ceiling of the utricle, while the other hangs sagittally on the wall of the saccule.

The afferent fibers in the superior vestibular nerve lead from the superior and horizontal SCCs, the utricle, and anterosuperior portion of the saccule. The inferior vestibular nerve innervates the posterior SCC and the saccule (Aw et al. 2001). Each vestibular nerve consists of about 26 000 bipolar neurons (Park et al. 2001), nuclei of which are located in Scarpa's ganglion near the brainstem (Lorente de Nó 1933). The vestibular nerve carries neural information to the vestibular nuclei: the SCC neurons terminate primarily in the superior and medial vestibular nuclei, and otolith organs project to the lateral, medial, and inferior vestibular nuclei (Gacek 2005).

2.2 ANATOMY OF THE CENTRAL VESTIBULAR SYSTEM

The central part of the vestibular system comprises the lateral, medial, superior, and inferior vestibular nuclei in the brainstem, their projections to the extraocular motor nuclei, the descending spinal cord, and the cerebellum. Vestibular projections via the brainstem to the oculomotor nuclei help maintain the stability of objects on the retina during head movement by producing an eye movement equal in magnitude, but opposite in direction, to a head movement (Minor 1998). The shortest pathway of the AVOR consists of three different neurons: first-order afferent neurons connect the hair cells with the four major and three minor vestibular nuclei in the brainstem. These neurons are connected with the nuclei of the III and VI cranial nerves by second-order interneurons in the brainstem. The third are ocular motor neurons to the external eye muscles (Figure 2) (Gacek 2005). The brainstem seems also to preserve SCC signals via

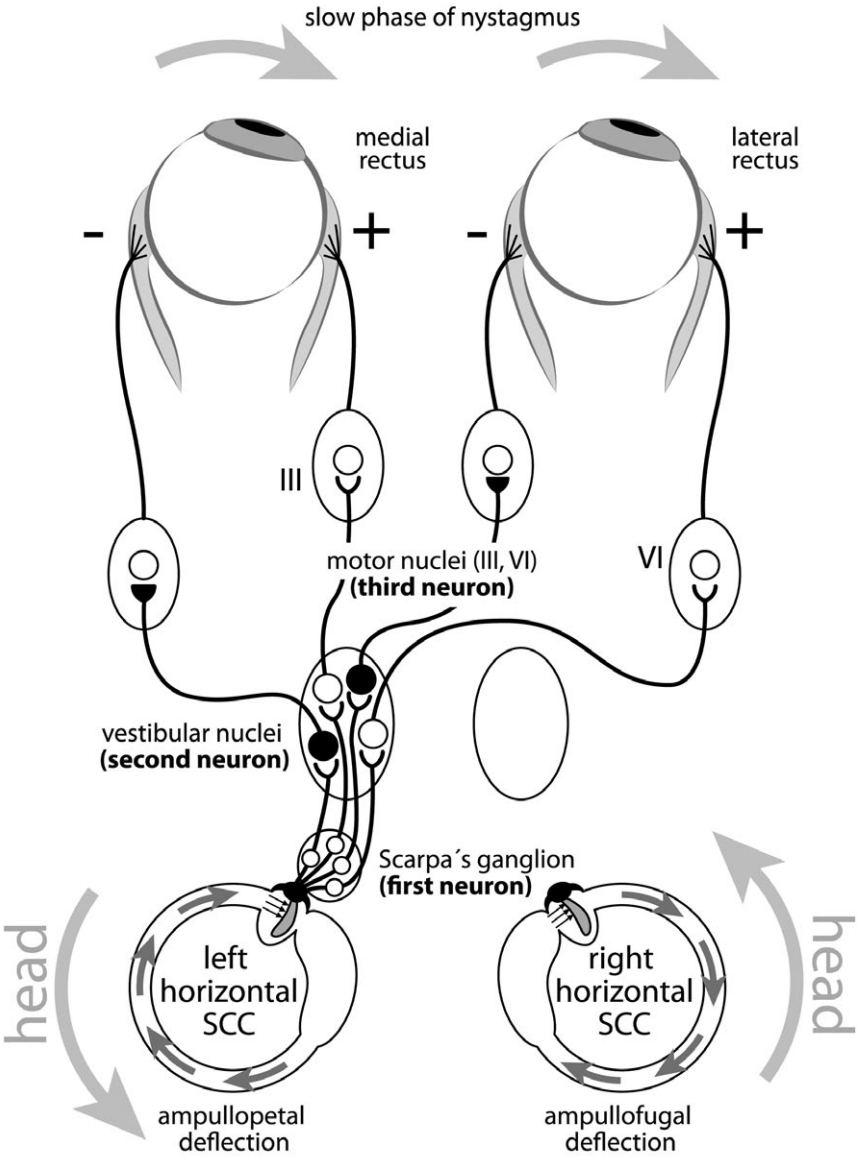

Figure 2. *Neural connections in the pathway of the horizontal AVOR. Head rotation to the left leads to endolymph flow towards the ampulla in the left horizontal SCC (excitation), and away from the ampulla in the right horizontal SCC (inhibition). Excitatory interneurons in the vestibular nuclei connect to the ocular motor neurons in motor nuclei (III, VI), which cause muscle contraction and pull the eyes to the right, opposite to the head direction. The influence of inhibitory interneurons on ocular motor neurons in motor nuclei III and VI causes the relaxation of antagonist muscles, which augments the eye movement.*

neural circuits between certain groups of neurons in the brainstem (Katz et al. 1991). These commissural connections modify the activity in the vestibular nuclei and make the cooperation of individual canal pairs possible.

Most vestibular inputs reach the spinal cord anterior horn cell through the lateral and medial vestibulospinal tract. The lateral vestibulospinal tract originates from the neurons of the lateral vestibular nucleus and descends ipsilaterally in the lateral funiculus into the cervical, thoracic, or lumbosacral cord. The medial vestibulospinal tract originates in the lateral, medial, and inferior vestibular nuclei and descends bilaterally in the medial longitudinal fasciculus to the cervical and upper thoracic cord level (Gacek 2005). Many neurons of that tract extend to the neck segments of the cervical spinal cord and to extraocular nuclei (Minor et al. 1990). Otolith-mediated postural reflexes are controlled mainly by the lateral vestibulospinal tract (Minor 1998). Close-loop vestibulo-collic reflexes, which stabilize the head in space by means of neck muscle activation, are thought to be mediated mainly by the medial vestibulospinal tract (Wilson and Schor 1999).

Central vestibular circuits include the cerebellum, which is involved in calibration and coordination of the head and eye movements (Lisberger 1998, Lysakowski et al. 1998). All aspects of the three-dimensional ocular motor response to head rotation are under the influence of the cerebellum (Walker and Zee 2005). The cerebellum is also highly interrelated to the vestibulospinal pathways (Baloh and Hornubia 2001a, Jacobs and Horak 2007).

The vestibular organs are represented in the cerebral cortex. Recent evidence in humans using functional magnetic resonance imaging indicates that the parietal and insular regions are the cortical locations in processing vestibular information (Brandt et al. 2002).

2.3 ORGANIZATION OF ANGULAR VESTIBULO-OCULAR REFLEXES

SCCs respond primarily to angular acceleration in the yaw, pitch, and roll planes. The otoliths sense primarily linear acceleration along each of these planes. The canal-based AVOR maintains a steady image on the retina while the head is turning. The otolith-mediated linear vestibulo-ocular reflex is responsible for head tilts and linear movements, and these pathways are much more complex than those for the canals. Although angular and linear vestibulo-ocular reflexes are detected by separate groups of receptors in the labyrinth, they are inherently interactive (Minor and Zee 1998).

Physiology

Goldberg and Fernández (1971) recorded in squirrel monkeys the fact that primary vestibular afferent neurons have spontaneous activity of about 90 to 100 spikes/s. While these firing rates can be driven upwards to 300 to 400 spikes/s, they can be inhibited no lower than 0 spikes/s. A large asymmetry thus exists between excitatory and inhibitory responses of a SCC. This observation is referred to as Ewald's second law (Ewald 1892). The neurophysiologic basis of this push-pull cooperation between the SCC pairs was further explained by Goldberg and Fernandez (1975) in monkeys, and confirmed in humans by Paige (1989), Halmagyi et al. (1990), and Lasker et al. (2000).

Visual-vestibular interaction

The AVOR interacts with three vision-based oculomotor systems: The optokinetic system stabilizes images whenever the entire visual world moves, the smooth pursuit system stabilizes smoothly moving targets of the fovea, and the saccadic system moves a target from the peripheral retina onto the fovea (Henn et al. 1980, Raphan and Cohen 1978). These non-vestibular systems operate optimally at low frequencies and during slow head movements. These reflexes overlap with the vestibular system for part of its operating range, but become largely ineffective during fast head movements (Carey and Della Santina 2005). Visual tracking usually has a latency of greater than 100 milliseconds (Krauzlis and Miles 1996), although the latency of refixation saccades during head thrusts can be as short as 70 milliseconds (Tian et al. 2000, Weber et al. 2008). The AVOR can be modified by altering the visual conditions, for example by adaptation of magnifying or minifying spectacles (Clendaniel et al. 2001), or by looking at a close or distant target (Collewijn and Smeets 2000, Crane and Demer 1998, Lasker et al. 2002).

Cervical-vestibular interaction

The cervico-ocular reflex, induced by the neck proprioceptors, employs proprioceptive information from the neck to stabilize the head on the body. Bárány (1906, 1918) first demonstrated that head torsion in the rabbit and in newborn infants produces eye deviations in the direction in which the body is twisted. The experimental work of de Jong et al. (1977) in humans showed gait deviation and a tendency to fall down after local anesthesia of neck tissue. In normal adults and in patients with unilateral vestibular hypofunction, the cervico-ocular reflex has a low gain and seems to make a negligible contribution to gaze stability, and only during low velocity head rotation (Barlow and Freedman 1980, Huygen et al. 1991, Sawyer et al. 1994, Schubert et al. 2004a).

Parameters

The AVOR is usually characterized by gain, asymmetry in gain, and latency. The perfect compensative eye movement during head movement requires a gain (eye velocity/head velocity) of unity, and the studies of AVOR responses to brief, unpredictable, dynamic, high-acceleration stimuli have shown that the gain is close to unity in healthy subjects (Aw et al. 1996b, Collewijn and Smeets 2000, Cremer et al. 1998, Halmagyi et al. 1990). In other words, the eyes rotate in the opposite direction with approximately the same speed as the head during angular head impulses. The vestibulo-ocular reflex can induce compensatory eye movement up to velocities of 350º/s (Pulaski et al. 1981, Roy and Tomlinson 2004). For velocities higher than this, the gain saturates (Roy and Tomlinson 2004). Velocities of head movements during daily natural locomotion do not exceed the velocity saturation limit of the vestibulo-ocular reflex (Grossman et al. 1988). For example, the mean velocities during walking or running are less than 100º/s (Grossman et al. 1989).

The asymmetry in gain between the sides ((gain right-gain left) / (gain right + gain left)) x 100% in normal subjects varies between 4 and 13% (Allison et al. 1997, Park et al. 2005, Weber et al. 2008). The latency of AVOR (time from beginning of head movement to onset of compensatory eye movement) is about 7 milliseconds (Aw et al. 1996b, Crane and Demer 1998, Lasker et al. 2002, Minor et al. 1999, Tabak and Collewijn 1994).

Pathophysiology

Disorders in AVOR can result in impaired compensatory eye movements in response to head movement, with consequent loss of visual acuity. The magnitude of the symptoms depends on whether the lesion is unilateral or bilateral, the rapidity with which the functional loss occurs, and the extent of the lesion (Baloh and Hornubia 2001a). For example, the slow growth of VS is usually accompanied by central compensation, though the patients may have no symptom.

After unilateral vestibular deafferentation, studies with transient passive head rotations have demonstrated permanent reduction in AVOR gain towards the ipsilateral side (Aw et al. 1996a, Cremer et al. 1998, Halmagyi et al. 1990, Weber et al. 2008). Only a slight loss of gain occurs on the contralateral side, which is due to the loss of disfacilitation of the operated side (Halmagyi et al. 1990, Weber et al. 2008). In contrast to unilateral vestibular deafferentation, in patients after vestibular neuritis, ipsilateral gain seems to improve over time (Palla and Straumann 2004). Most patients with an AVOR deficit use saccades in order to refixate the target lost during head movement (Cremer et al. 1998, Peng et al. 2005, Tian et al. 2000).

Bilateral peripheral loss of vestibular function can lead to permanent oscillopsia, the perception that stationary objects are moving (Brandt and Strupp 2005). This condition can be very disabling and lead to major restriction of the patient's motion (Grossman and Leigh 1990, JC 1952).

2.4 ORGANIZATION OF POSTURAL REFLEXES

The major function of the vestibulospinal reflexes is to keep the head and body stable in space. Although the organization of the vestibulospinal reflexes is principally the same as that of the AVOR, the postural control is considerably more complicated. Even a simple movement requires a complex response of contraction and relaxation in multiple antigravity muscles of the neck, trunk, and extremities (Baloh and Hornubia 2001a).

The inherently unstable upright stance in humans require corrective action based on information from three sensory modalities: Visual (Bronstein 1986), vestibular (Johansson et al. 1995), and somatosensory (Jeka et al. 1997, Popov et al. 1996). Vestibular input is referenced to gravity, while somatosensory and visual inputs are referenced to earth-based support and visual surround (Mirka and Black 1993). Neck proprioceptors signal head-on-body position, whereas otoliths signal head-in-space position (Schwarz and Tomlinson 2005). El-Kahky et al. (2000) calculated the contribution of all the different senses to posture in healthy subjects: maximal labyrinthine input was up to 44%, visual input to 37%, and minimal proprioceptive input to 26% under the different sensory conditions measured with dynamic posturography. Most quantitative investigations of postural control are based on the body's center of gravity (COG) and sway calculation (Baloh et al. 1998, Cohen et al. 2002).

Disorders of the vestibulospinal reflex can result in tilt of the head, abnormal posture, or ataxia. On an unstable surface, subjects increase sensory weighting towards vision and vestibular information. Patients with peripheral vestibular loss are limited in their ability to re-weight postural sensory dependence and in certain sensory conditions are at risk of falling (Horak 2006). It is difficult to define a disease-specific pattern for sensory dependence, since it shows strong individual variance (Lacour et al. 1997).

2.5 VESTIBULAR SCHWANNOMA

The VS is the most common cerebello-pontine angle tumor of the VIII cranial nerve, and it arises from the internal auditory canal (Komatsuzaki and Tsunoda 2001, Nager 1985). Evidence from the recent literature indicates that VS arises in almost half the cases from the inferior portion of the vestibular nerve (Frommeld et al. 1998, Slattery et al. 1997). In a study from Japan, the appearance of VS in the inferior portion of the vestibular nerve was over 80% (Komatsuzaki and Tsunoda 2001). However, topographic work on cadavers has shown no clear morphologic evidence for specifying tumors as in the superior or inferior vestibular nerve, except in the lateral fundus of the internal auditory canal (Terasaka et al. 2000).

Hearing loss is the most common initial symptom in about 75% of patients with VS preoperatively (Kentala and Pyykko 2001, Rosenberg 2000). Imbalance is the main preoperative symptom in 10 to 19% of cases (Driscoll et al. 1998, Humphriss et al. 2003, Kentala and Pyykko 2001). The vestibular symptoms are rarely severe (Driscoll et al. 1998, Lynn et al. 1999, Parietti-Winkler et al. 2006). In contrast, most patients have severe vertigo and postural instability immediately after tumor removal due to sudden loss of vestibular nerve function (Cohen et al. 2002, Darrouzet et al. 2004). These symptoms seem to be relieved within a month (Cohen et al. 2002, Lynn et al. 1999, Mruzek et al. 1995). Three months after surgery, 30 to 65% of patients still have had mild symptoms of balance disturbance (Darrouzet et al. 2004, Levo et al. 2004, Wiegand et al. 1996). A positive head thrust sign may remain permanent (Foster et al. 1994).

2.6 CLINICAL TESTS OF ANGULAR VESTIBULO-OCULAR REFLEXES

Head thrust test

The oculocephalic response (Doll's eye reflex) has served for many years for evaluation of comatose patients (Fisher 1969). Two decades ago, Halmagyi and Curthoys (1988) first described the occurrence of this response in patients who had undergone unilateral vestibular neurectomy, elicited with rapid, transient, horizontal head rotation toward the lesioned side. The manually delivered HTT allows bedside identification of unilateral hypofunction of the peripheral vestibular system (Brandt and Strupp 2005, Carey and Della Santina 2005, Demer et al. 2001). The HTT identifies catch-up saccades after sudden head rotations, which are indirect signs of the AVOR deficit (Weber et al. 2008). In

recent studies, the sensitivity and specificity of "bedside" HTT has been about 70% compared to the quantitative head impulse test, measured with magnetic search coils; the authors thus found the HTT clinically useful (Jorns-Haderli et al. 2007, Kessler et al. 2008). According to Brandt and Strupp (2005), no complementary caloric irrigation is necessary with a clear pathological finding in an HTT.

Although the HTT is useful to identify acute unilateral peripheral vestibular deficit, it is considerably less sensitive in patients with chronic, compensated, and incomplete unilateral lesions (Beynon et al. 1998, Bronstein 2003, Halmagyi 2004). Moreover, in a recent study of Newman-Toker (2008), of 30 patients with cerebellar stroke 9%, and in Cnyrim et al. (2008) as high as 39% of acute central vestibular pathology showed a positive HTT. Thus, this test is not fully specific for peripheral vestibular pathology. Furthermore, visual detection, whether or not fast refixation catch-up saccades occur, may be difficult (Foster et al. 1994, Schmid-Priscoveanu et al. 2001, Weber et al. 2008). These early covert saccades cannot be distinguished from a residual AVOR response while the head is still moving, because the head impulse lasts only about 150 milliseconds (Schmid-Priscoveanu et al. 2001, Weber et al. 2008). In addition, proper training is necessary to perform and evaluate the HTT correctly (Halmagyi et al. 2001, Schubert et al. 2004b), and the HTT should be repeated to identify catch-up saccades correctly (Foster et al. 1994, Weber et al. 2008).

Cold caloric test

Irrigation with ice water into the ear canal induces nystagmus. In a normal subject, the duration and speed of this nystagmus varies greatly, but > 20% asymmetry in nystagmus duration can be a sign of a lesion on the side of the decreased response (Baloh and Hornubia 2001b).

2.7 LABORATORY TESTS OF ANGULAR VESTIBULO-OCULAR REFLEXES

Measurements of eye movements

Electro-oculography

Electro-oculography (EOG), a technique based on corneoretinal potential, has been the method most widely used in clinical vestibular laboratories. It is noninvasive, easily administered, cost-effective, and reasonably accurate for

horizontal eye movements (Baloh and Hornubia 2001b). EOG permits recording of the direction, amplitude, and velocity of the eye movement (Fife et al. 2000). This technique allows recording of ± 40º horizontal, and ± 20º vertical eye movements with an accuracy of about 1º, but it does not measure torsional eye movements (Bhansali and Honrubia 1999, Brandt and Strupp 2005).

Disadvantages of EOG include its poor signal-to-noise ratio, its sensitivity to eye-blink artifacts and the repeated need for calibration due to the fluctuation of the corneoretinal dipole potential (Baloh and Hornubia 2001b, Proctor et al. 1980, Wuyts et al. 2007).

Magnetic search coil

MSC is a technique that has been called the gold standard in experimental ocular motor recording due to its extremely detailed recording of horizontal, vertical, and also torsional movements in all three planes (Newman and Lambert 2005, Wuyts et al. 2007). This technique, developed by Robinson (1963), is based on measurement of electric current induced in a fine copper coil embedded in a contact lens and placed on the eye under local anesthesia. The MSC technique gives very high-resolution data with an accuracy of about 0.2º (Hullar et al. 2005). It is affected less by eyelid movement than EOG and has a much larger vertical range (Foster et al. 1997).

The major disadvantage of this technique is the need to wear a wired contact lens in the anesthetized eye, causing discomfort for the patient, and therefore the recording time is limited to approximately 20 to 30 min (Brandt and Strupp 2005, Wuyts et al. 2007). Additionally, because sophisticated equipment is involved, and the cost of the procedure is high, the MSC technique is used mainly as a research tool in certain academic centers (Brandt and Strupp 2005, Fetter 2000, Hullar et al. 2005, Wuyts et al. 2007).

Video-oculography

Video-oculography is a commercially available computer-based system to record eye movements non-invasively and without dependence on facial muscle artifacts as in EOG (Bojrab and Ostrowski 2005). Two-dimensional video-oculography enables registration of horizontal and vertical eye movements, and three-dimensional video-oculography can additionally follow the torsional component of eye position (Schworm et al. 2002, Zingler et al. 2006).

However, most commercial video-oculography systems have a low sampling rate of 50 to 60 Hz compared to 500 to 1 000 Hz for search coils. This limits the

identification of saccades (Houben et al. 2006, Wuyts et al. 2007). The video-oculography seems, however, to have an accuracy comparable to that of the MSC technique in recording of nystagmus of patients with peripheral vestibular deficit (Houben et al. 2006, Imai et al. 2005, Jorns-Haderli et al. 2007).

Caloric test

The bithermal caloric test has remained one of the cornerstones of vestibular function testing. It allows testing of both ears independently, and the stimuli can be applied relatively easily with a technique that is commonly available (Bhansali and Honrubia 1999, Prepageran et al. 2005). Separate investigation of each labyrinth makes it possible to calculate the peripheral unilateral weakness of the AVOR, the upper normal limit of which ranges between studies from 20 to 31% (Brandt and Strupp 2005, Fife et al. 2000, Park et al. 2005, Perez and Rama-Lopez 2003, Schmid-Priscoveanu et al. 2001).

Caloric irrigation predominantly stimulates the horizontal SCC, and thus provides little information about other SCCs (Wuyts et al. 2007). The caloric test provides only a non-physiological stimulation of the horizontal SCC with a frequency up to 0.004 Hz, which is far lower than natural frequencies of the head movements during walking and running (0.7-8 Hz), and well below the ideal operating range of the AVOR (150-300º/s) (Halmagyi et al. 1990, Schmid-Priscoveanu et al. 2001, Prepageran et al. 2005). The caloric response may vary depending on the patient's alertness (Davis and Mann 1987) and individual variation in temporal bone anatomic features (Davidson et al. 1988).

Preoperative unilateral weakness has been pathologic in 50 to 70% of patients with VS (El-Kashlan et al. 1998a, Enticott et al. 2005, Frommeld et al. 1998, Humphriss et al. 2003). In contrast, pathologic unilateral weakness has been present in all acute patients with vestibular neuritis, although in only 60% of chronic patients (Schmid-Priscoveanu et al. 2001).

Rotational tests with sinusoidal head oscillations

Obvious advantages of rotational tests over caloric testing are that the patient's responses from rotational testing do not depend on the effectiveness of thermal energy transfer, and they allow precise application of multiple frequencies of natural, rotational stimuli (Fife et al. 2000). One of the main disadvantages of rotational testing is that rotation affects both ears simultaneously, making it less helpful in detecting unilateral lesions (Brandt and Strupp 2005, Fife et al. 2000).

Rotational chair test

The rotational chair test, in which the patient's head and body move in unison, is a commercially available motor-generated passive test. The most commonly used rotation test protocol is the slow harmonic acceleration test, which operates at oscillation frequencies of 0.01 to 0.64 Hz with a peak sinusoidal velocity of 50º/s. (Bojrab and Ostrowski 2005).

However, these frequencies and accelerations of conventional sinusoidal testing are too low for detection of unilateral vestibular hypofunction (Collewijn and Smeets 2000, Halmagyi et al. 2001); this test is therefore most useful in assessing patients with bilateral vestibular hypofunction and patients receiving vestibulotoxic medication (Hullar et al. 2005). Sinusoidal chair rotation at higher frequencies (up to 11 Hz) and velocities (up to 120º/s) have made only a small diagnostic contribution compared to that of a caloric, HTT, or quantitative head impulse test (Kessler et al. 2008). Furthermore, predictive steady-state rotational stimuli may lead to eye movement responses arising from non-vestibular mechanisms such as somatosensory or central prediction mechanisms (Wiest et al. 2001). Due to the high price of this equipment (Fife et al. 2000), dependence of the measures on the patient's mental alertness (Wuyts et al. 2007), and head slippage during testing (Hanson and Goebel 1995), clinical use of the rotational chair is limited.

Head autorotation test

The head autorotation test requires an active sinusoidal head oscillation by the subject, with frequencies of 2 to 6 Hz (Hirvonen et al. 1997b, Meulenbroeks et al. 1995, O'Leary et al. 1991). Unless the head autorotation test has a relatively low cost, is repeatable, and is well tolerated by most patients (O'Leary and Davis 1994), it would not appear to be useful in detecting unilateral peripheral vestibular loss (Fife et al. 2000). In addition, sinusoidal rotations in a head autorotation test may allow complementary non-vestibular inputs to contribute to the response, and this can artificially enhance AVOR function (Della Santina et al. 2002, Hirvonen et al. 2000, Hoshowsky et al. 1994).

Postoperatively, 58% of patients with VS had an abnormal gain (between 0.85 and 0.60), measured with the head autorotation test up to velocities of 4 Hz (Hirvonen et al. 2000).

Rotational tests with transient head impulses

Quantitative head impulse test

Halmagyi et al. (1990) demonstrated a markedly asymmetric AVOR gain in patients after unilateral vestibular deafferentation, elicited with passive, rapid, transient head rotations. These angular "head impulses" are unpredictable, high-velocity, high-acceleration, and low-amplitude head rotations. Low-velocity and low-frequency rotation are insufficiently dynamic to cut off responses in the inhibited nerve (Halmagyi et al. 2001, Paige 1989). Passive head impulses are better for demonstrating a unilateral vestibular deficit. In contrast, active impulses produce a higher AVOR gain and generate earlier compensatory saccades (Black et al. 2005).

The patient, seated upright, is instructed to fixate on a light-emitting diode target at a distance from about 90 to up to 150 cm (Aw et al. 1996, Black et al. 2005, Jorns-Haderli et al. 2007). The examiner, standing behind the subject, holds the subject's head and delivers randomized rapid head impulses, from five to forty impulses to each side (Della Santina et al. 2002, Schmid-Priscoveanu et al. 2001). The eye and head positions were measured with the MSC technique, in which a contact lens is placed either on one or on each eye (Carey et al. 2002, Prepageran et al. 2005). Head displacement is recorded with the MSC fixed tightly on the forehead, upon the nose-piece of spectacle frames, or mounted onto a dental impression bite bar (Aw et al. 1996b, Jorns-Haderli et al. 2007, Lehnen et al. 2004).

The amplitude of head impulses was between 10 and 20º. The head velocities and accelerations varied considerably among studies, from 50 to 500º/s, and from 1 500 up to 10 000º/s², respectively (Black et al. 2005, Cremer et al. 1998, Jorns-Haderli et al. 2007, Kessler et al. 2008, Lasker et al. 2002).

The quantitative head impulse test was the most accurate method for characterization of unilateral vestibular deficiency compared to the HTT and head autorotation test (Della Santina et al. 2002). Testing of AVOR with the quantitative head impulse test appeared to provide valuable additional diagnostic information on patients with persistent imbalance, compared to HTT, caloric and, rotational chair tests (Kessler et al. 2008). However, manually delivered impulses are inherently variable across time and experimenters, and the head velocities are highly variable (Collewijn and Smeets 2000, Tabak et al. 1997a, Wiest et al. 2001). Advantages and disadvantages of the MSC registration technique, used in the quantitative head impulse test, were discussed above.

Test results

In healthy subjects, the gain value was between 0.94 and 1.02 (Aw et al. 1996b, Cremer et al. 1998, Halmagyi et al. 1990, Weber et al. 2008). The normal asymmetry in gain was between 4 and 13% (Allison et al. 1997, Park et al. 2005, Weber et al. 2008). Latency has differed between 7 and 11 milliseconds in healthy subjects (Aw et al. 1996b, Della Santina et al. 2002).

Several studies which evaluate postoperative gain include a limited number of patients after unilateral vestibular deafferentation. With peak head velocity from 100 to 300º/s and peak acceleration from 1 500 to 4 000º/s², the gain was markedly reduced on the ipsilateral side, and a slight loss of gain occurred on the contralateral side: 0.2 to 0.4 and 0.55 to 0.85, respectively (Aw et al. 1996a, Carey et al. 2002, Cremer et al. 1998, Halmagyi et al. 1990). With higher peak acceleration, the decrease in ipsilateral gain value was even more profound: 0.13 to 0.18 with acceleration up to 6 000º/s² (Black et al. 2005, Weber et al. 2008). The asymmetry in gain has varied between 25 and 65% in patients after unilateral vestibular deafferentation (Carey et al. 2002, Weber et al. 2008).

Rotational test with whole-body stepper motor

Studies with transient stimuli have been sparse partly because of technical limitations of the conventional rotational devices (Collewijn and Smeets 2000, Goebel et al. 1995). Crane and Demer (1998) have developed a more powerful device for impulse rotation, the whole-body stepper motor (500 Nm). The illuminated target was located 15 or 500 cm in front of the subject's right eye. During the test, the subject's head, body, and feet were secured via multiple belts to a chair mounted on the servomotor, which elicited 10 rotations in both directions (Demer et al. 2001). The eye position was measured with the MSC technique, whereas head movement was measured by a search coil mounted in a bite bar. This rotator received a peak stimulus velocity of 190º/s and acceleration of 2 800º/s², and it rotated the head 40º in 250 milliseconds (Tian et al. 2000, Tian et al. 2001, Wiest et al. 2001).

As an advantage of testing AVOR with transient whole-body rotation, the authors have mentioned the more controllable stimulus than in the quantitative head impulse test (Demer et al. 2001). A disadvantage is the variation in head movement, common for the highest stimulus due to greater decoupling of the head from the rotator (Crane and Demer 1998, Hanson and Goebel 1995).

In a healthy subject, the AVOR gain at a target distance of 500 cm was 0.68 and at a distance of 15 cm, 0.84; the latency was between 5 and 10 milliseconds (Crane and Demer 1998, Tian et al. 2000). The postoperative ipsilateral AVOR gain in patients with VS at a target distance of 500 cm was 0.37 versus 0.78 on the contralateral side (Tian et al. 2000).

Reactive torque helmet

Tabak and Collewijn (1994) have introduced a reactive torque helmet as a technique for more homogenized head impulses. The subject, seated upright, is instructed to fixate on a light-emitting diode target at a distance of about 120 cm. A driver-powered torque motor is placed on top of the helmet, which is suspended via a spring from the ceiling. The head and eye movements are recorded with the MSC technique, in which the head movement sensor coil is attached to the custom-made bite board.

A trial included 20 head displacements in each direction (Tabak and Collewijn 1994). The motor on the helmet rotated the head through amplitudes from 10 to 20º, and reached peak head velocities of 80 to 150º/s and accelerations of 700 to 1 500º/s² (Collewijn and Smeets 2000, Tabak et al. 1997a, Tabak et al. 1997b).

The authors found the helmet technique superior to their manually delivered steps, because the helmet provides uniform acceleration (Collewijn and Smeets 2000, Tabak et al. 1997a). The reactive torque helmet reached, however, relatively low transient head velocities and acceleration (Wiest et al. 2001).

In healthy subjects, the average AVOR gain was between 0.9 and 1.01 (Collewijn and Smeets 2000, Tabak and Collewijn 1994, Tabak et al. 1997a), and latency was between 5 and 9 milliseconds (Collewijn and Smeets 2000, Tabak et al. 1997a). In 35 patients with VS, the mean postoperative ipsilateral gain was 0.59 ± 0.07 standard deviation (SD) versus 0.94 ± 0.11 SD on the contralateral side (Tabak et al. 1997b). The asymmetry in gain of these patients was between 20 and 24%.

2.8 CLINICAL TESTS OF POSTURE

The **Romberg test** (Romberg 1846) is used to assess body sway with feet together or in tandem with eyes either open or closed. Bárány (1907) noticed the importance of the vestibular influence in maintaining the Romberg position, because patients with an acute vestibular lesion swayed or fell in the direction of the damaged side. However, increased swaying can also occur in healthy subjects, and this test cannot distinguish between vestibular deficit and other causes (Baloh et al. 1998, Hall and Herdman 2005).

The **Unterberger stepping test** was introduced by Unterberger (1938), who was the first who studied the tendency of a unilateral vestibular lesion to induce a turn in the earth-vertical axis while walking in place. The more sophisticated

Fukuda stepping test (Fukuda 1959) can similarly show subject's turning toward the side of a unilateral vestibular lesion. This test gives poor test-retest reliability, however (Bonanni and Newton 1998).

The **tandem gait test** is widely used as a part of the routine neurological examination. When performed with eyes open, tandem walking is primarily a test of cerebellar function. Falls in the tandem gait test, eyes closed, are indicative of peripheral vestibular dysfunction (Hullar and Minor 2005). The test results are nonspecific, and some healthy subjects are unable to succeed in this test (Baloh and Hornubia 2001b).

2.9 LABORATORY TESTS OF POSTURE

A method to record human postural sway employs a computerized commercial or custom-built force platform, dual plates with either three or four load cells (Snijders and Verduin 1973, Starck et al. 1992). Each of these platforms is designed to measure the position of the center point of forces during an upright stance, which is a good estimate of the position of the subject's COG if the body is moving slowly (Baloh and Hornubia 2001b, Geurts et al. 1996).

Static posturography

Static posturography records postural sway in an immobile position on a static force platform. It involves Romberg's test with eyes open or closed (Norre 1994). The results of static posturography are derived from changes in the center point of forces amplitude or velocity, and the outcome is compared with the performance of healthy subjects (Baloh and Hornubia 2001b, Levo et al. 2004). A quiet stance may be disturbed by various sensory conflicts, for example vibration of the calf muscles, or cooling of the soles of the feet (El-Kahky et al. 2000, Hafstrom et al. 2002).

The major limitation of static posturography is that it is unable to isolate the relative contribution of sensory modalities during the maintenance of an upright stance, and it does not provide stimulus-response measurements of postural sway (Baloh and Hornubia 2001b, Di Fabio 1996, Harcourt 1995). Static posturography has been suggested for monitoring the balance of one patient sequentially, but not for comparison between subjects, due to the large interindividual variance (Uimonen et al. 1994).

In patients with VS, mean sway velocity had almost returned to its preoperative value three months after surgery, but in many patients it did not reach normal values even after one year (Levo et al. 2004).

Dynamic posturography

Nashner (1971) developed the concept of dynamic posturography more than three decades ago, and the equipment became commercially available in 1986 as the "Equitest". The sensory organization test has been the most useful test for dynamic posturography (Furman 1994). In the sensory organization test, postural sway can be measured under conditions in which visual and somatosensory feedback is altered: the first two test conditions are as in the standard Romberg tests, and the remaining four conditions involve sway-referenced displacement of the platform, vision, or both to "isolate" vestibular function (Cass et al. 1996, Cohen et al. 2002, Mruzek et al. 1995, Nashner 1993). Anterior-posterior sway of the COG is monitored. Equilibrium scores are determined as a ratio of the actual body sway to a theoretical maximum required for stability, where 100% represents perfect stability (Mruzek et al. 1995).

Shumway-Cook and Horak (1986) supplied a force platform with a foam-rubber pad and used a moving screen with a Japanese lantern to provide a visual conflict situation. The results of this "foam and dome" test were well comparable to those with dynamic posturography (El-Kashlan et al. 1998b). To date, quantitative computerized posturography on foam is commercially available (Amin et al. 2002, Rama-Lopez et al. 2004).

A specialist panel (American Academy of Neurology 1993) concluded that dynamic posturography had a promising role in the assessment of balance-disorder patients, but later this conclusion has been questioned (Dobie 1997, Evans and Krebs 1999). During postural sway in dynamic posturography, several parts of the vestibular labyrinth are simultaneously stimulated, and for that reason their individual function cannot be isolated (Baloh and Hornubia 2001b). The findings of dynamic posturography are often non-specific, and it therefore cannot isolate the underlying dysfunction (Brandt and Strupp 2005). In one review article (Di Fabio 1995) the sensitivity of posturography in detecting peripheral vestibular deficit was low, about 50% for dynamic and static posturography. A large inter-individual and intra-individual variance exists in normal body sway with dynamic posturography (Baloh et al. 1994, El-Kahky et al. 2000). In addition, data from dynamic posturography can be strongly influenced by patient effort, fatigue, cognition, and the impact of instruction (El-Kahky et al. 2000, Hall and Herdman 2005). The commercially available equipment for dynamic posturography is expensive, as is per test cost (El-Kashlan et al. 1998b, Evans and Krebs 1999).

In a study by Parietti-Winkler et al. (2006), patients with VS showed preoperatively in the fifth condition of the sensory organization test abnormally low equilibrium scores (vision unavailable and sway-referenced support surface). During one month after surgery, postural control had rapidly recovered to close to preoperative level, and the follow-up three months postoperatively showed further improvement in postural control but did not reach the normal level. Comparable results in patients with VS have been reported by Cohen et al. (2002). In addition, dynamic posturography has served as a quantitative measure of balance, especially in follow-up of the rehabilitation process (Black et al. 2000, Cass et al. 1996, Furman 1994, Hall and Herdman 2005).

Visual feedback posturography

VFP, known also as the limits of stability test, was introduced two decades ago as a tool for practicing postural control and evaluating rehabilitation for patients with hemiplegia or cerebellar ataxia (Shumway-Cook et al. 1988, Jobst 1989). VFP integrates use of the sensory input from visual, proprioceptive, and vestibular sense organs for postural control (Amin et al. 2002, Hamann and Krausen 1990, Jobst 1990). The subject, standing on a static force platform, receives immediate visual feedback of his or her postural forces by watching the movement of a COG marker on a computer screen (Hall and Herdman 2005). The screen displays the COG location and a series of visual targets positioned generally at eight places around the circle at either 75 or 100% of stability limits (Clark et al. 1997, El-Kashlan et al. 1998b, Hamman et al. 1992). In the commercially available Balance Master force plate, the stability limits are determined by use of standing height and fixed maximum leaning angles of healthy subjects (12º in the anterior-posterior direction and 16º in the lateral direction) (Duncan et al. 1990, Hamman et al. 1992). Posture is evaluated by various parameters of COG movement, as for example, transition time, direction control, end point COG excursion, movement velocity, and extent of the path (Clark et al. 1997, Geurts et al. 1996, Hamman et al. 1992, Sihvonen et al. 2004).

The overall reliability of VFP ranged from moderately high to high with stability limits of 75 and 100% in elderly subjects (Clark et al. 1997). Among nine- and ten-year-old children, the VFP showed fair to good reproducibility (Geldhof et al. 2006). Sihvonen et al. (2004) applied VFP with good success in balance training of elderly subjects. VFP has been suggested as a tool to predict the risk for falling among elderly subjects (Pajala et al. 2008). Barclay-Goddard et al. (2004) reviewed standing balance training with VFP after stroke, and concluded, however, that there is no clear evidence that VFP training improves clinical balance outcomes.

3. AIMS OF THE STUDY

The objectives of this study were to evaluate the applicability (1) of visual feedback posturography for quantification of postural control, and (2) of a motorized head impulse rotator in characterization of the angular vestibulo-ocular reflex.

The specific aims were:

1. To determine the repeatability of VFP, and to determine the normative limits for postural control, especially for side difference (I).

2. To assess with VFP the postural control in patients with VS, to compare the VFP results with those of a caloric test and with subjective balance disturbance (II, III), and to examine the side difference in patients' postural control (II).

3. To evaluate a quantitative motorized head impulse test (MHIT) in assessment of horizontal AVOR and to determine normal values for the AVOR parameters (IV).

4. To explore the feasibility of MHIT for evaluation of horizontal AVOR in patients with VS (V).

4. SUBJECTS AND METHODS

All studies were approved by the ethics committee of the Helsinki University Central Hospital.

4.1 SUBJECTS

In Study I, 23 healthy volunteers (mean age 39; range 16–54 years) were measured with a custom-made VFP five times on different days within a median period of 2 weeks. The interval between individual test sessions ranged from 1 to 12 days (mean 3 days).

In Study II, active postural control was measured 1 to 3 days before the surgery in 49 consecutive patients with unilateral VS with VFP, treated at Helsinki University Central Hospital between 1999 and 2003. The patients comprised 20 men and 29 women with a mean age of 49 (range 30-67) years. Of these VS patients, 36 repeated VFP about 3 months postoperatively, and 47% of them were additionally tested about 1 month after surgery (*Study III*). A retrosigmoid approach was used for all except one patient, who underwent a middle fossa approach.

In Study IV, the horizontal AVOR was tested twice with a motorized head impulse rotator in 22 healthy volunteers (5 men and 17 women), mean age 42 (range 27-59) years. For evaluation of gain increase at a short target distance, 8 subjects underwent additional testing.

In Study V, the AVOR was prospectively followed with the MHIT in 38 consecutive patients with unilateral VS operated on at Helsinki University Central Hospital between 2004 and 2006. The preoperative group comprised 19 men and 19 women, mean age 49 years (range 33–69). The test was performed one day before the operation, and after the surgery via a retrosigmoid approach 71% of patients repeated the test between 3 and 12 months (mean 4.3 months).

4.2 METHODS

Equipment and measurement

Visual feedback posturography (Studies I-III)

Active postural control was measured with a custom-made force platform similar to that of Snijders and Verduin (1973). It comprised three load cells (type Z8, Hottinger Baldwin Messtechnik GMBH, Darmstadt, Germany) situated in a triangular pattern, placed 4.65 cm from each other, underneath the platform. The analysis software was developed further from an earlier force platform construction and was running in a Hewlett-Packard work station (HP 9 000 series 300, type 340) (Starck et al. 1992). The instantaneous position of the center point of forces was calculated by signals from the three load cells, and a COG marker was displayed on the computer screen, at a location analogous to the center point of forces position at a rate of 50 Hz.

The center of the computer screen was 132 cm above the platform surface. Each subject stood on the platform with feet positioned medially and with his heels against a wooden support mounted on the platform surface, with their arms crossed on their chest (Figure 3). The subjects' COG was displayed as a 2 x 2 mm marker on a computer screen 65 cm in front of them. The subjects could move the COG marker in the required direction by leaning their body on the platform. Subjects were instructed to move their COG marker as accurately and fast as possible from the central target to the eight peripheral targets and to keep the marker inside the target as long as it was visible.

The targets were displayed one by one in an alternating but constant order of appearance (Figure 4). The size of each of the eight targets on the computer screen matched an area of 2 x 2 cm on the platform surface, and each was visible for 15 s. To facilitate the return to a neutral position, a central area appeared for 5 s between appearances of each target. The anterolateral, lateral, and posterolateral targets were located symmetrically on the left and right sides. The anterior and the posterior targets were vertical along the center line.

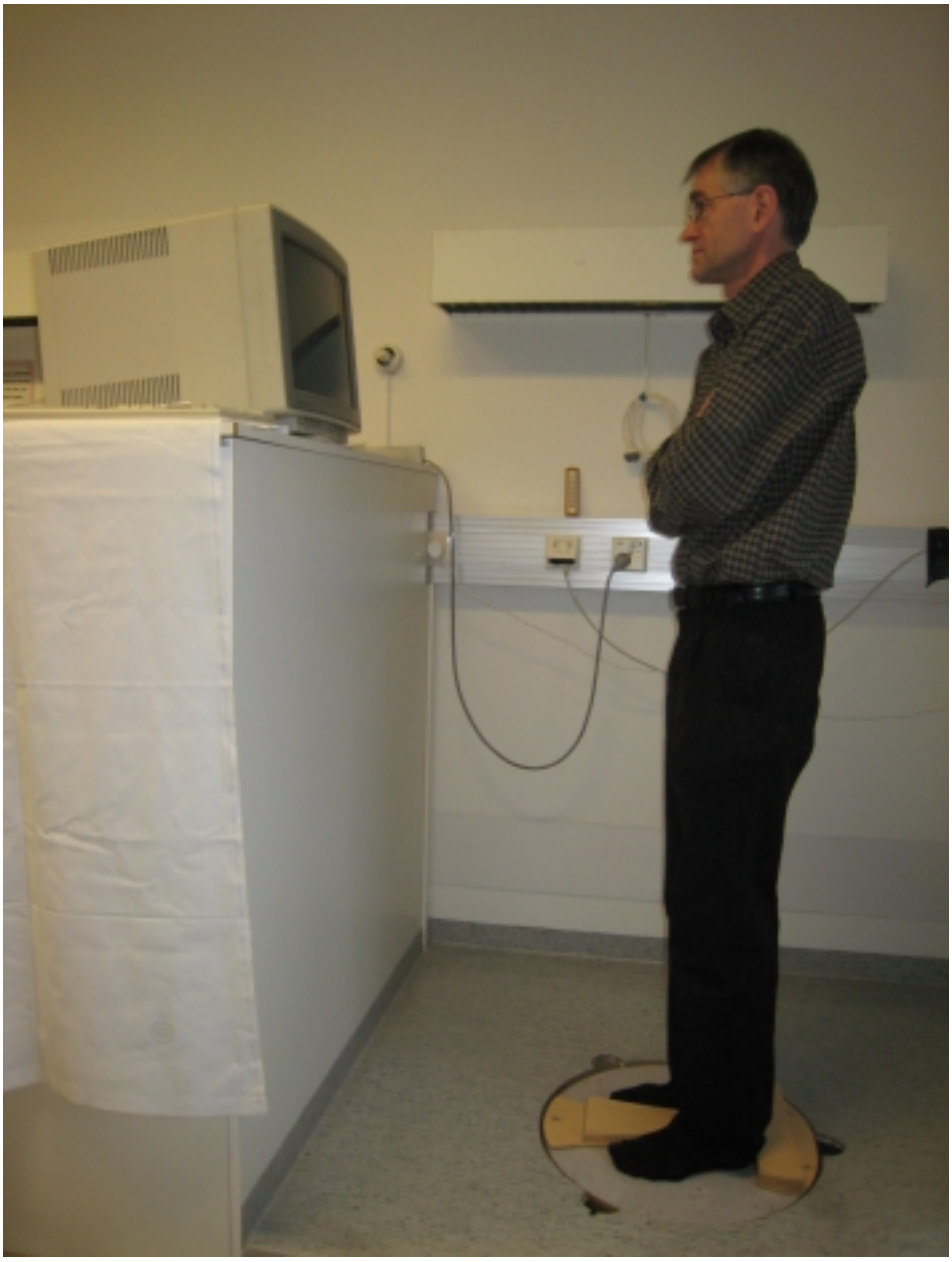

Figure 3. *Visual feedback posturography. While standing on the force platform, the subject moves his COG marker, displayed on the computer screen, in the direction required by leaning his body.*

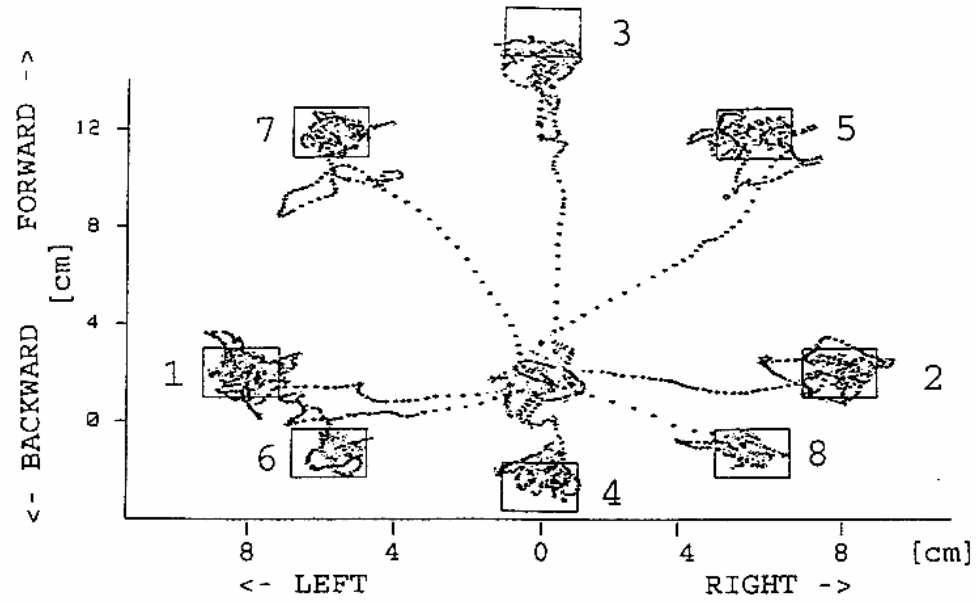

Figure 4. *Example of the VFP recording in a healthy subject, showing targets and paths of the COG marker to the targets. Targets in front of the subject's neutral, resting position are uppermost and targets behind the neutral position lowermost. The order of target appearance is shown beside each target.* *(Reprinted from the original article with the permission of copyright holder, S. Karger AG, Basel: Hirvonen M, Aalto H, Hirvonen TP. Preoperative postural control of patients with vestibular schwannoma assessed by visual feedback posturography. ORL J.Otorhinolaryngol.Relat.Spec. 68(4):232-236, 2006).*

The target distance from the center of the screen was 50% of the subjects' calculated stability limits, which were proportional to the shoe size of each patient. Individual stability limits were calculated with the software before the VFP, and their determination was based on an experiment in healthy controls (Hirvonen et al. 1997a). Each test session included four practice runs at different difficulty levels (40-80% of the stability limits and either 1 × 1 or 2 × 2 cm peripheral targets), and the test run at the end of the session.

Motorized head impulse test (Studies IV-V)

For investigation of AVOR we used a motorized head impulse rotator developed for this project, in which horizontal head-on-body rotations were generated by a motor and gear combination (DC-motor GR 63 x 25, and planetary gear PLG 52.0, Dunkermotoren, Alcatel SEL AG, Bonndorf, Germany). This combination was fixed to the back-rest of a rigid chair with a rotating plate attached to the axle. The rotations were delivered to the joints on both sides of a tightly fastened leather helmet with two pushrods from the rotating plate (Figure 5). The helmet could be individually fitted in the horizontal and oblique planes by tightening of plastic belts from an industrial worker's safety helmet. The turning angle was mechanically limited to ± 30º for safety reasons. The top of the helmet was stabilized with a rotating joint to a supporting bar, which eliminated anteroposterior movement of the head. Two additional supporting rods were attached to the bar and the chair, to lessen unnecessary lateral movement.

The torque impulse was obtained by driving the motor with a pulse of increasing voltage fed to a motor driver (LA-5600, linear drive amplifier, Electro-Craft Corporation, Motor & Control System Division of Robbins & Myers, Minneapolis, MN, USA) (Aalto et al. 2002). The proper pulse waveform was determined experimentally to produce an approximately linear velocity increase during the first 120 milliseconds with constant acceleration (up to 2 000º/s^2) for each impulse. Active braking came from reversed driving voltage to the motor. The return to the starting position was accomplished by driving the motor at a slower pace.

The subject, seated upright, was instructed to fixate at the light-emitting diode target at a distance of 140 cm on the midline and at eye level. The head was positioned comfortably within the helmet. While the subject fixated at the target, his head was rotated in the horizontal plane. The impulses were randomized in direction and in time interval between impulses (range, 1.0-1.4 s). These passive transient head rotations had (mean ± SD) an acceleration of 1 550 ± 240º/s^2, peak head velocity of 170 ± 27º/s, and amplitude of 21 ± 3º. The average duration from the beginning of the head impulse to the peak head velocity was 120 milliseconds. Each test lasted 80 s and consisted of 23 impulses in each direction (left and right).

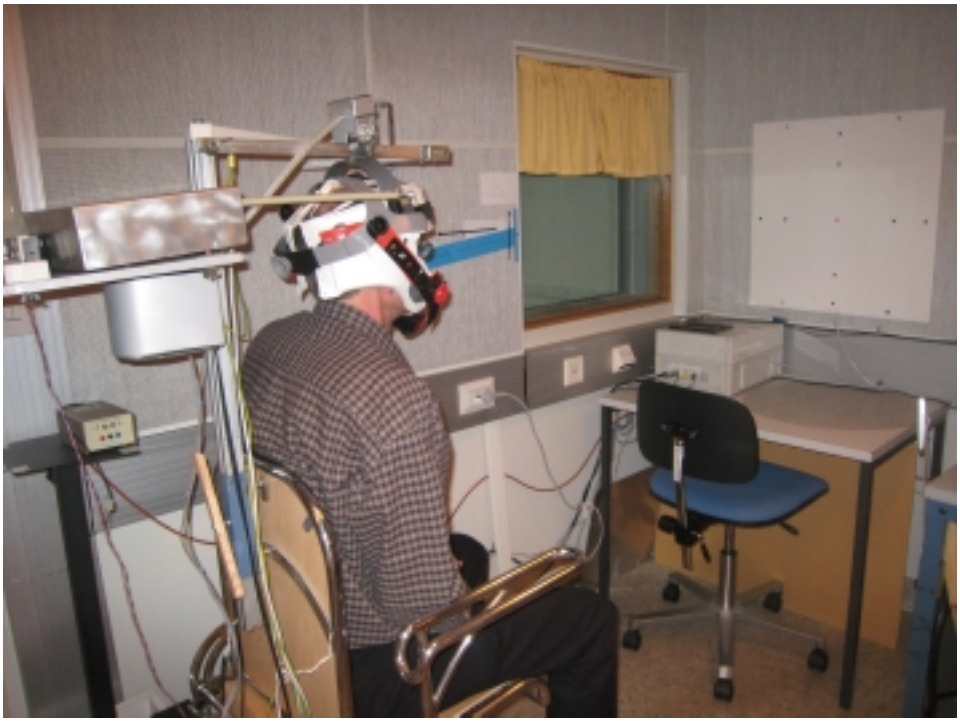

Figure 5. *The motorized head impulse test. While seated, the subject wears a tightly fitted elastic helmet and fixates his gaze at the light-emitting diode target at a distance of 140 cm. Eye movements are recorded with electro-oculography and head movements with a rotation angle sensor. Head impulses are generated randomly to each side with the motorized head impulse rotator.*

The head position was measured with a rotation-angle sensor (type CP-2UT; Midori Precisions Co, Ltd, Tokyo, Japan), which was directly attached to the helmet. The noise velocity of the sensor was less than 0.1º/s. Eye position was monitored via EOG. Two active electrodes were attached to the lateral canthi of the eyes, and the ground electrode was mounted on the forehead. The EOG signal was amplified and low-pass filtered with a cut-off frequency of 30 Hz before the analog-to-digital conversion. The eye and head movement signals were recorded with a sampling frequency of 400 Hz and a 16-bit resolution. Before analysis, the EOG signal was further low-pass filtered with a cut-off frequency of 10 Hz. The noise velocity of the EOG signals was < 5º/s. Eye movement was calibrated before each test by recording horizontal saccades of ± 10º.

Analysis

Visual feedback posturography (Studies I-III)

Hit delay (HD) to the targets (s), hold percentage (HP) within the targets (%), COG marker velocity (CMV) to the targets (cm/s), and balance index (BI) (s/%) were calculated as a mean of the eight individual targets. The HD was measured as the time used to move the COG marker from the central target to the peripheral target. The HP was computed as the ratio of the holding time inside to the appearance time of the peripheral target, after the target was first reached. The CMV was calculated as the path length of the COG marker divided by the HD. The BI was calculated by dividing the HD by the HP. The primary purpose of introducing the BI was to obtain a single parameter which combines both the velocity and the accuracy of postural control for clinical use. Asymmetry between the sides (%) was determined by comparing the mean BI of right-sided targets to that of left-sided targets. In Study III, in addition, sway velocity (SV) within the targets (cm/s) was calculated.

Motorized head impulse test (Studies IV-V)

The processed eye and head movement signals were fed into a data analysis program (Eye Movement Analyzer, version 37; Migliaccio, A.) written in the LabView program, version 7.1 (National Instruments, Austin, TX, USA). Data with prominent noise or artifacts that commenced before the onset of the head movement were manually discarded from analysis. Impulses with velocities $< 100^{\circ}$/s and with eye velocities $> 20^{\circ}$/s at the beginning of the head movement were excluded. The start of head movement was determined as the time when head velocity reached 10°/s.

The AVOR gain, asymmetry in gain, and latency were calculated. The AVOR gain was calculated by dividing eye velocity by inverted head velocity. The gain was calculated during the 30-millisecond period before peak head velocity, and in the period when head velocity ranged from 100 to 120°/s. To quantify the asymmetry in gain of the response to left and right rotations, asymmetry was defined by the following equation: asymmetry in gain = ((gain contralateral - gain ipsilateral) / (gain contralateral + gain ipsilateral)) x 100%. Latency was calculated as the time difference in milliseconds between the head and eye reaching the threshold velocity of 10°/s.

Clinical and other vestibular examination

In Studies II and III, the preoperative and postoperative subjective balance disturbance was retrieved by retrospective analysis of the patients' medical case notes. We rated intensity of balance disturbance on a 5-point qualitative scale (1 = none, 5 = severe). In Studies II and V, all patients underwent the electronystagmography test. For the caloric test, unilateral weakness < 30% was considered normal. In Study V, all patients completed a questionnaire preoperatively and postoperatively regarding their subjective balance disturbance, hearing, and quality of life on a 5-point qualitative scale for each factor (1 = none or just perceptible symptoms, 5 = disabling symptoms).

Statistics

In Studies I and III, the statistical difference between subsequent test sessions was determined by analysis of variance with individual comparisons made by the Bonferroni test. Intraclass correlation coefficients and probabilities were computed to evaluate the repeatability of the VFP test. In Studies II, III, and V, preoperative and postoperative test results were compared with each other and with those of the healthy control group by the t-test, assuming unequal variances. The non-parametric Spearman rank correlation test (II, V) and Kendall rank correlation test (III) were used to examine the correlation between test parameters and other patient characteristics. In Study IV, the non-parametric Pearson rank correlation test served to compare the AVOR gain values measured from two different parts of the head impulse curve. The gains at different target distances were compared with the t-test for paired samples.

Statistical calculations were performed with SPSS software, version 11.0 (SPSS Inc., Chicago, IL, USA). A p value < 0.05 was considered statistically significant.

5. RESULTS

5.1 VISUAL FEEDBACK POSTUROGRAPHY (I – III)

Healthy subjects (I)

An example of a VFP recording for a healthy volunteer is illustrated in Figure 4. The targets are the rectangular figures. The paths between the central area and the targets are quite straight, but unsteadiness of the COG marker near the targets is visible.

The mean VFP results are shown in Table 1. The mean BI and HD decreased significantly during five repeated test sessions between the first and fourth/fifth tests ($p < 0.05$), but they did not change significantly between other test sessions. The length of the time interval between subsequent test sessions did not correlate significantly with the respective change in the BI ($r = 0.19$; $p = 0.08$). The mean CMV and the mean HP did not change significantly during repeated testing. The intraclass correlation coefficients for all parameters during these sessions were significant ($r = 0.93$-0.96; $p < 0.01$). The normative range (mean ± 2 SD) for the BI was < 2.5 s/%, and for the asymmetry 22%.

Table 1. *Mean VFP results ± 95% confidence interval (CI) for repeated tests in healthy controls (N = 23).*

VFP parameters	Test session				
	1	2	3	4	5
BI (s/%) *	1.7 ± 0.2	1.5 ± 0.2	1.4 ± 0.2	1.2 ± 0.2	1.3 ± 0.2
CMV (cm/s)	6.9 ± 1.3	8.4 ± 1.7	10.0 ± 2.8	10.8 ± 2.6	11.6 ± 3.6
HD (s)*	1.6 ± 0.2	1.4 ± 0.2	1.3 ± 0.2	1.2 ± 0.2	1.2 ± 0.2
HP (%)	95.3 ± 1.2	95.6 ± 1.5	96.3 ± 1.1	97.1 ± 0.9	96.8 ± 0.9

**p < 0.05: statistically significant improvement between 5 subsequent test sessions. Abbreviations: BI, balance index; CMV, COG marker velocity to targets; HD , hit delay to targets; HP, hold percentage within targets.*

Patients (II, III)

Figure 6 demonstrates a VFP recording before surgery of a patient with VS. The paths to the targets are irregular, and remarkable unsteadiness is notable, especially close to the rear targets at the bottom of the figure.

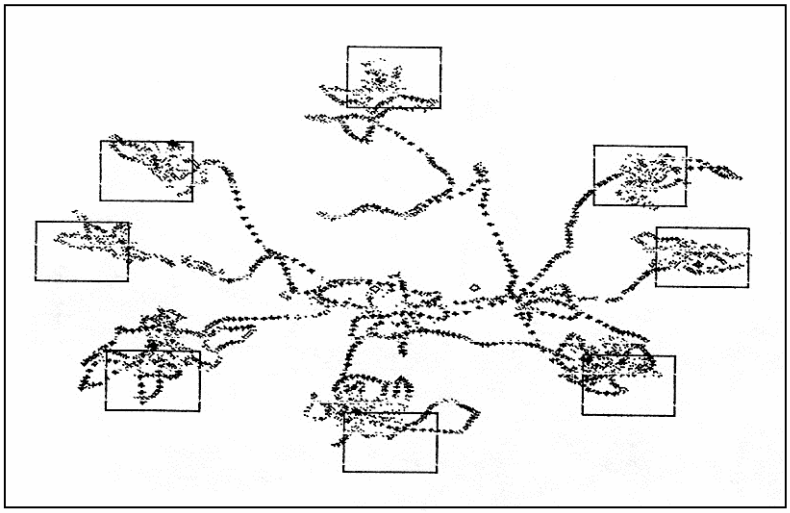

Figure 6. *An example of VFP recording in a patient with unilateral vestibular schwannoma before surgery, with eight rectangular targets and paths of the COG marker to these targets. Unsteadiness both in the paths to the targets and in the hold within the targets is clear.* *(Reprinted from original article with the permission of copyright holder, S. Karger AG, Basel: Hirvonen M, Aalto H, Hirvonen TP. Postural control after vestibular schwannoma resection measured with visual feedback posturography. ORL J.Otorhinolaryngol.Relat.Spec. 67(6):335-339, 2005).*

A comparison between VFP test results in patients with VS and healthy individuals is in Table 2. The SV and the BI were significantly increased, and the HP was significantly reduced in patients with VS before and after surgery compared to those of healthy controls: a respective preoperative $p = 0.009$, 0.005, and < 0.001; one month postoperative $p = 0.004$, 0.002, and 0.002; three months postoperatively $p = 0.016$, 0.031, and 0.017. The HD was increased among patients preoperatively ($p = 0.023$), and at 3 months postoperatively it also tended to be increased ($p = 0.066$), compared to the control group. The CMV did not differ significantly between patient- and control groups.

Table 2. *Mean results of VFP ± 95% CI for controls (N = 23) and patients (preoperatively, N = 49; one month and three months postoperatively, n = 17 and 36) with vestibular schwannoma during three repeated test sessions.*

VFP parameters	Controls, 1st test	Patients, 1st test	Controls, 2nd test	Patients, 2nd test	Controls, 3rd test	Patients, 3rd test
BI (s/%)	1.7 ± 0.2	2.1 ± 0.3*	1.6 ± 0.2	2.0 ± 0.2*	1.4 ± 0.2	1.9 ± 0.3*
SV (cm/s)	1.6 ± 0.2	2.0 ± 0.2*	1.7 ± 0.2	2.3 ± 0.4*	1.8 ± 0.2	2.1 ± 0.2*
HP (%)	95.3 ± 1.1	90.8 ±2.0*	95.6 ± 1.4	91.3 ± 2.4*	96.3 ± 1.0	91.9 ±2.7*
HD (s)	1.6 ± 0.2	1.9 ± 0.3*	1.4 ± 0.2	1.6 ± 0.3	1.4 ± 0.2	1.7 ± 0.2
CMV (cm/s)	6.9 ± 1.2	6.6 ± 0.9	8.4 ± 1.6	9.0 ± 2.0	10.0 ± 2.6	8.2 ± 1.4

** $p < 0.05$: statistically significant difference between the groups. Abbreviations: BI, balance index; SV, sway velocity within targets; HP, hold percentage within targets; HD, hit delay to the targets; CMV, COG marker velocity to targets.*

At least one VFP parameter was abnormal preoperatively in 45%, and in 47% of patients 3 months after surgery. All the postural control parameters except SV tended to improve postoperatively, even though this was not significant. The abnormal preoperative VFP results correlated significantly with the abnormal postoperative VFP results ($r = 0.56$; $p = 0.001$). The intraclass correlation coefficients in repeated VFP measurements in 17 individual patients were significant ($r = 0.78$-0.96; $p < 0.001$).

The side difference in patients with VS (mean ± 95% CI) of 11.6 ± 3.2% was not statistically significant compared with that of 9.2 ± 2.2% in healthy individuals ($p = 0.229$). A significant side difference appeared in only 10% of patients.

Preoperatively, on the day of the clinical examination, 49% of patients expressed a subjective balance disturbance (33% just perceptible, 4% mild, 12% moderate). As 12% of the patients had experienced a balance disturbance before the examination, a total of 61% of the patients had experienced a balance disturbance preoperatively. Three months after surgery, 45% of the patients experienced a subjective balance disturbance (28% just perceptible, 11% mild, 6% moderate). No correlation appeared between the presence of pre- and postoperative subjective balance disturbance.

Before surgery, the HD and the BI correlated significantly with subjective balance disturbance ($p = 0.02$ for both), whereas after surgery this correlation was absent for all VFP parameters. The unilateral weakness, which was abnormal in 59% of the patients with VS, did not correlate significantly with the VFP results or with subjective balance disturbance.

5.2 MOTORIZED HEAD IMPULSE TEST (IV, V)

Healthy subjects (IV)

In healthy subjects, compensatory eye movements matched closely the head movements. The mean AVOR gain within the 30-milliseconds interval before peak head velocity and at head velocities ranging from 100 to 120º/s was 1.08 ± 0.10 SD (Table 3). The correlation between individual gain values measured from these two different parts of the impulses was significant ($r = 0.72$; $p < 0.001$). The mean gain, normalized for the target distance with the constant 1.065, was 1.02 ± 0.09 SD. In eight subjects, measured with different target distances, the mean gain at a target distance of 15 cm was significantly higher than at a target distance of 140 cm (1.26 versus 1.07; $p = 0.002$). Mean asymmetry in gain was 3.7 ± 2.8% SD. Mean latency was 3.4 ± 6.3 milliseconds SD.

Table 3. *Mean AVOR gain ± SD in 22 healthy subjects within 30 milliseconds before peak head velocity (I) and at a head velocity range of 100 to 120º/s (II). Gains during analysis windows I and II did not differ significantly (p > 0.05).*

Analysis window	Gain to right	Gain to left	Gain in both directions
I	1.10 ± 0.10	1.06 ± 0.11	1.08 ± 0.10
II	1.10 ± 0.09	1.06 ± 0.12	1.08 ± 0.10

Patients (V)

Both AVOR parameters, gain and asymmetry in gain, were simultaneously abnormal in 34%, and at least one parameter was abnormal in 71% of the patients.

Gain

Of the 38 patients, 45% had normal gain preoperatively on both sides (Figure 7). For example, in one of these patients, eye movements elicited by head impulses towards the affected side were almost identical. This pattern is consistent with the AVOR of healthy subjects.

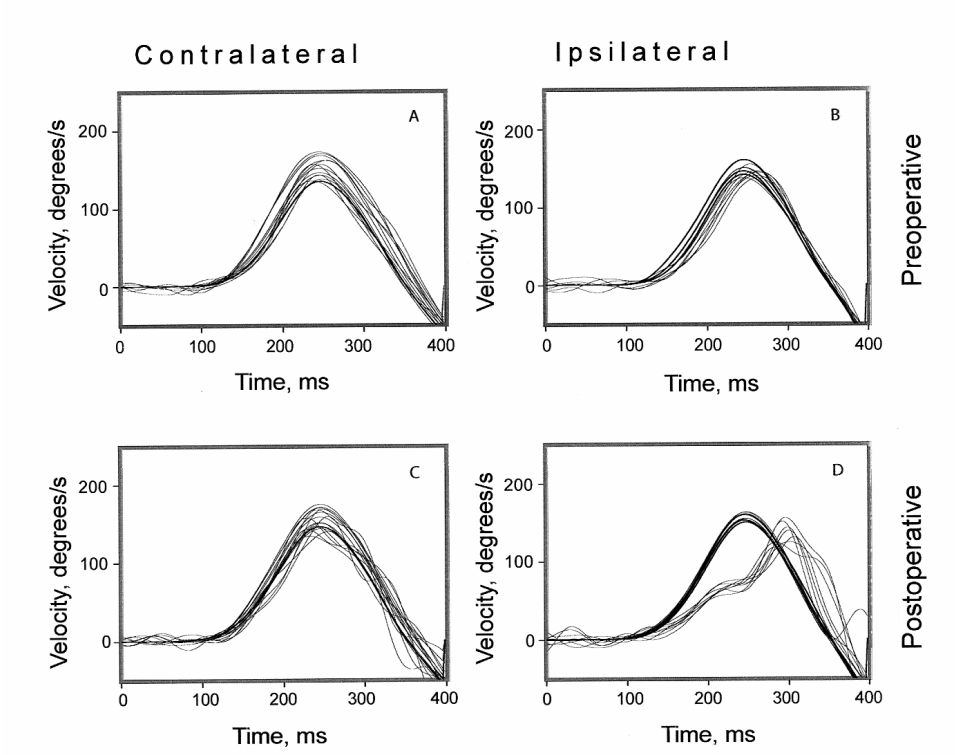

Figure 7. *Horizontal AVOR recording in a patient with unilateral VS, impulses delivered by motorized head impulse rotator. Panels A and B: recording of a patient with symmetrical preoperative findings. Panel C recording shows a close to normal postoperative recording from the contralateral side, whereas panel D shows an ipsilateral profound gain decrease with late refixation saccades.* *(Reprinted from the original article with the permission of copyright holder, Taylor & Francis: Hirvonen M, Aalto H, Hirvonen TP. Motorized head impulse rotator in patients with vestibular schwannoma. Acta Otolaryngol.(Stockh) 128(11):1215-1220, 2008).*

Table 4. *Comparison of AVOR gain (mean ± 95% CI) in patients with vestibular schwannoma before and after surgery.*

Side	Preoperative	Postoperative	p value
Ipsilateral	0.83 ± 0.08	0.53 ± 0.05	< 0.001
Contralateral	0.98 ± 0.06	0.87 ± 0.06	0.02

$p < 0.05$: statistically significant difference between groups.

The mean preoperative AVOR gain on the ipsilateral side (0.83 ± 0.08 95% CI) was significantly lower than in healthy controls ($p < 0.001$). The mean preoperative gain on the contralateral side (0.98 ± 0.06) was close to normal, but it also differed significantly from that of healthy controls ($p = 0.02$). Postoperatively, all 27 patients had abnormal gain on the ipsilateral side, and for almost half of them the gain was significantly decreased on the contralateral side, as well.

The AVOR responses after unilateral tumor removal are in Figure 7. A clear postoperative deficit is evident on the operated side with a plateau in the eye velocity signals (velocity saturation area), and thereafter compensatory saccades to refixate the eyes on the target. This kind of velocity plateau was noticeable in 70% of the patients on the operated side. On the contralateral side, the configuration of eye movement signals resembles that of normal responses. The postoperative gains (mean ± 95% CI) on the operated side of 0.53 ± 0.05 and on the contralateral side of 0.87 ± 0.06 were both significantly reduced compared to corresponding preoperative values (Table 4).

Asymmetry in gain

Half the patients showed abnormal preoperative asymmetry in gain (mean ± 95% CI) of 19.1 ± 5.1%. The mean asymmetry in gain of the entire group of patients was significantly increased compared to that of healthy controls ($p < 0.001$). All patients showed increased asymmetry in gain after tumor removal. The postoperative asymmetry in gain compared to the preoperative value was significantly increased to 24.8 ± 3.5% ($p < 0.001$).

Other findings

Unilateral weakness in the caloric test was abnormal in 59% of patients. Preoperatively, a highly significant correlation appeared between the unilateral weakness and asymmetry in gain ($r = 0.54$; $p < 0.001$). The unilateral weakness and AVOR test results before and after surgery had no statistically significant correlation with subjective balance disturbance.

The preoperative quality of life was significantly influenced by the subjective sensation of hearing level ($r = 0.48$; $p = 0.004$), but it showed no correlation with subjective balance disturbance. The postoperative quality of life was significantly influenced by balance disturbance ($r = 0.68$; $p < 0.001$).

6. DISCUSSION

Healthy subjects and patients with unilateral VS were measured with VFP for evaluation of posture, and with a motorized head impulse rotator for evaluation of horizontal AVOR.

The repeatability of VFP was good, although the small learning effect seen in healthy volunteers must be considered when evaluating postural control with VFP. VFP could not detect the lesioned side in most patients with unilateral loss, and this assumption of side detection in a posturography technique proposed recently also by Brandt and Strupp (2005) remains to be proven viable. Pre- and postoperatively in patients with VS the mean accuracy of active postural control, compared to that of healthy controls, was reduced. The inaccuracy of active postural control persisted after surgery in most of those patients with preoperative VFP abnormalities.

To our knowledge, the MHIT was the first technique using motorized head impulses and noninvasive eye movement recording (EOG) in evaluation of the AVOR. Our construction showed relevant results for evaluation of normal vestibular function and of pathological responses among patients with unilateral VS. The preservation of preoperative AVOR function in patients with VS has not yet been systematically addressed by use of a HTT. The horizontal AVOR measured with the MHIT was preserved in approximately one-quarter of patients on the operated side preoperatively, whereas it remained abnormal in every patient about four months after surgery.

6.1 VISUAL FEEDBACK POSTUROGRAPHY

Methodological aspects

The subjects performed four practice runs during each VFP session before the actual measurement in order to familiarize themselves with the test, and they were instructed to perform the test as accurately and fast as possible. These details in measurement design are important for reducing the learning effect and variation in the results (Clark et al. 1997). Hamman et al. (1992) reported a significant learning effect in healthy subjects up to the third and fourth VFP test session at 75% of the subject's stability limits. This would not be suitable for the follow-up measure, due to the difficulty in distinguishing between learning and a rehabilitation effect. We used a difficulty level of 50% of stability limits to

reduce the chance of a possible learning effect. The BI and the HD showed significant improvement only between the initial and the fourth/fifth test sessions. This learning effect, however, must be taken into account when interpreting these VFP results. On the other hand, our low difficulty level may have reduced VFP sensitivity. Our VFP study with VS patients showed that almost half the patients with VS had preoperatively (45%) and postoperatively (47%) at least one abnormal VFP parameter. This percentage reflects the sensitivity of VFP. It is close to the review result of Di Fabio (1996), in which the sensitivity of posturography in detecting peripheral vestibular deficit was about 50% for dynamic and static posturography.

In the present study with controls, intervals between test sessions were usually a few days, although for five subjects, some of the intervals were longer than one week. However, the length of time interval between test sessions had no significant effect on our VFP results, even including those with a noticeable learning effect. Hamman et al. (1992) tested healthy individuals with VFP five times, either once a day or once a week. Their significant improvement during repeated tests was independent of whether the test sessions were repeated daily or weekly. VFP may thus be performed confidently at various intervals.

We introduced the BI as a simple measure of postural control which combines both the velocity and the accuracy of postural stability. In our VFP studies of patients with VS, VFP parameters such as BI, HP, and SV significantly differed both before and after surgery compared to those of healthy controls, whereas HD and CMV did not differ significantly. This implies that in patients with VS the accuracy is more affected than is the velocity of postural control movements. Moreover, the disturbance in postural control seems to be more pronounced in distant, challenged targets for postural control.

General aspects

Clark et al. (1997) studied 38 elderly adults with VFP and found that the reliability during three measurements varied from moderately high to high with stability limits of 75 and 100%. In our study, the repeatability of VFP was high in 23 healthy subjects during five test sessions ($r = 0.93\text{-}0.96$; $p < 0.01$), and good in 17 individual patients during three test sessions ($r = 0.78\text{-}0.96$; $p < 0.001$). Variance between subjects in VFP can, however, be quite large. This fact suggests that VFP can be used serially to follow up the functional state of active postural control in individual patients rather than in between the patients.

The feet of the subjects were positioned symmetrically on each side by a wooden support, and the left- and right-sided targets were symmetrically located on the screen. This feature of VFP made it possible to evaluate the side difference in postural control by comparing responses for each side. The normative range

calculated as the mean ± 2 SD for the asymmetry was 22%. Although the body has a tendency to lean towards the affected side, a significant side difference in our patients with VS was rare. It occurred in only 10% of patients. This can be explained by the fact that each side of the vestibular end organ is not challenged separately during the VFP test. Thus, the subjects tend to keep their heads quite still during the tests, and the postural control movements towards both sides utilize bilateral vestibular information.

Before and after surgery, the mean VFP results of patients with VS compared to those of the healthy controls were disturbed, but they did not significantly change after surgery. This indicates that if the operation caused any worsening in postural control, it was compensated for, and was close to the preoperative level during the first postoperative month. Restoration of the neural activity between vestibular nuclei starts to take place three to four days after unilateral vestibular deafferentation (Curthoys 2000). Likewise, vestibular compensation has been demonstrated to occur mostly during the first weeks or month after vestibular neurectomy (Cass et al. 1991, Cohen et al. 2002, Mruzek et al. 1995, Parietti-Winkler et al. 2006). Most VFP parameters tended to improve postoperatively, even though three months after surgery 47% of the patients still had at least one abnormal VFP parameter. This finding is similar to postoperative measurements in VS patients with dynamic and static posturography (Cohen et al. 2002, Levo et al. 2004, Parietti-Winkler et al. 2006).

We found a statistically significant correlation among patients with VS between abnormal pre- and postoperative VFP. This finding is in line with findings of Cass et al. (1991), who showed that abnormality in dynamic posturography before unilateral vestibular deafferentation was preserved in the late postoperative period. Thus, this abnormality in the VFP may be an indication for more aggressive rehabilitation to normalize this disturbed postural control.

Miscellaneous

According to retrospective analysis of our patients' medical case notes, 61% of patients preoperatively, and three months postoperatively 45% had at least some problems with balance. These results are in close agreement with the respective balance disturbance rate of 50 to 65% and 30 to 65%, reported in studies based on different questionnaires and retrospective medical chart reviews (Darrouzet et al. 2004, El-Kashlan et al. 1998, Humphriss et al. 2003, Lynn et al. 1999). The unilateral weakness in the caloric test was abnormal in 59% of our patients, which was slight lower than the 63 to 70% reported by El-Kashlan et al. (1998a), Humphriss et al. (2003), and Kentala and Pyykkö (2001).

Of four VFP parameters, two had a significant correlation with subjective balance disturbance preoperatively, whereas the unilateral weakness did not. Although abnormality in postural control postoperatively did not agree with subjective balance disturbance, we can assume that VFP takes into account more than only the peripheral vestibular system in the evaluation of functional postural control. Unilateral weakness is irrelevant in evaluation of a VS patient's overall postural control. Moreover, the caloric test evaluates the horizontal SCC only and therefore rarely reflects damage to the inferior vestibular nerve (Frommeld et al. 1998, Komatsuzaki and Tsunoda 2001, Stipkovits et al. 1999).

6.2 MOTORIZED HEAD IMPULSE TEST

Methodological aspects

We made no comparison with manual impulses, but we assumed that the stimulus intensity is better controlled with motorized than with manual impulses. Our motorized head impulse rotator delivered during a test session 23 impulses on each side, randomized in direction and in time interval between impulses, with a mean peak head velocity of 170º/s and a mean acceleration of 1 550º/s^2. In the quantitative head impulse test, the examiner, standing behind the subject, held the patient's head and manually delivered various numbers (5-40) of randomized rapid head impulses to each side. Tabak et al. (1997a) compared motorized and manual impulses, and they found that motorized impulses resulted in more uniform acceleration than manual ones, although overall results agreed. Furthermore, the head velocities in a quantitative head impulse test have been highly variable among studies and even during individual test sessions, ranging from less than 100 to 500º/s (Black et al. 2005, Cremer et al. 1998, Jorns-Haderli et al. 2007, Kessler et al. 2008). Thus, the magnitude of manual impulses is inherently variable across time and experimenters, which must be taken into account when comparing results among studies. Accordingly, a more standardized approach using a precise stimulus profile should be superior.

Our equipment reached head velocities similar to the dynamic range of normal head movements during walking and running (Grossman et al. 1988). Tabak and Collewijn (1994) and Tabak et al. (1997a, 1997b) first used the helmet-driven torque motor with the MSC technique to evaluate the horizontal AVOR during head impulses. They achieved well-controlled transient impulses with a mean acceleration of 770º/s² and velocities of 50 to 100º/s during their analysis window. Their stimulus intensities during the time window of 90 milliseconds in the analysis were close to the eye velocity saturation of 50 to 75º/s seen in patients with vestibular abnormalities (Cremer et al. 1998), which should

diminish the difference between a normal and abnormal gain, and consequently, the test's usefulness. Our mean stimulation magnitude of 170º/s was well above this saturation range, which should allow a more accurate distinction between normal and even partial lesions in the horizontal AVOR. Roy and Tomlinson (2004), comparing velocity ranges of manual head impulses, found that velocities up to 200º/s produced the most repeatable results. Our findings are in agreement: all of our healthy subjects underwent testing twice to evaluate the repeatability of the measurement, and the correlation between the two consecutive measurements was high ($p = 0.004$) with an average 6% variance in gain within subjects.

Thus far, all quantitative tests of vestibulo-ocular reflex evaluation (quantitative head impulse test, whole-body stepper motor, and reactive torque helmet) have used a MSC for eye and head movement recording as the most precise recording technique of eye movements. The major disadvantage of this technique is the need to wear a wired contact lens in the anesthetized eye. Instead of this sophisticated and time-demanding method, we chose conventional EOG to record eye movements, owing to its noninvasive and easy set-up with surface electrodes. The disadvantage of EOG is its low resolution of approximately 1º compared to the MSC technique with about 0.2º, and its relatively high signal-to-noise ratio. The impedance of electrodes was checked before and after each test session, and on rare occasions, electrodes with high impedances were reattached or changed. Calibration in the EOG technique may vary depending on duration of the test and lighting of the room. The interval between the calibration and the test itself was kept as brief as possible (less than a minute) and the room dimly lighted to eliminate these sources of error. The VOR is adapted to spectacles, and therefore, all subjects were expected to use theirs during recordings. Sometimes a subject forgot to use her glasses, which ultimately distorted absolute gain values. We could use a calibration value from the other test of the subject as a comparison, and in addition, we used a slow sinusoidal head rotation of less than 0.5 Hz during fixation on the target at the end of each test to ascertain that the calibration value was accurate. Generally, there was no significant error with the calibration, but in single occasions the calibration value had to be corrected up to 10-15%.

Careful placement was necessary to minimize undesired movement of the electrodes and leads during testing. Subjects were instructed to be as relaxed as possible to avoid unwanted, but inevitable electromyographic noise from face muscles. Thus, filtering of the eye movement signal had to be effective to eliminate high-frequency noise, and a low-pass filter with a cut-off frequency of 10 Hz was applied to the signal before velocity conversion. Impulses with prominent noise were discarded from analysis (details in Methods). This issue was examined in detail with a subset of subjects, and revealed that removal of individual impulses had a negligible effect on results. This finding probably is owing to the fact that averaging a group of impulses for each side effectively

reduces the impact of a single impulse. In sum, traditional EOG seems to be effective in recording horizontal AVOR.

One adaptation method for unilateral vestibular defect is to restrict head movement towards the lesioned side (Halmagyi et al. 1990). Houben et al. (2005) suspected that neck movement involvement would be a significant limitation for the torque helmet technique. In our study with VS patients this mechanism should have caused a lower stimulation profile for impulses towards the ipsilateral side. However, velocities between the sides did not differ significantly, indicating that patients with a partial or total vestibular lesion are unable to limit their head movement during randomized, passive head impulses. Likewise, stimulation intensity did not differ significantly between our control subjects and patients.

Gain

Healthy subjects

The average AVOR gain for responses to brief, unpredictable, high-velocity impulses is close to unity, measured by the quantitative head impulse test and the reactive torque helmet (Aw et al. 1996b, Cremer et al. 1998, Halmagyi et al. 1990, Lasker et al. 2002, Tabak et al. 1997a, Weber et al. 2008). This value is analogous to our normal gain value with its mean of 1.08 ± 0.10 SD (normal range 0.88-1.28, mean ± 2 SD).

In the quantitative head impulse test, the AVOR gain was mostly calculated during a 30- to 50-milliseconds period, prior to the peak head velocity as representative of the "best value" for gain (Carey et al. 2002, Cremer et al. 1998, Park et al. 2005, Weber et al. 2008). Because of individually variable factors such as neck stiffness during head impulses or the weight of the head, the final head velocity in a group of subjects is never uniform, despite a similar stimulus intensity delivered to the helmet. Therefore, we also analyzed both -- gain during the 30-millisecond interval before peak head velocity, and gain in the head velocity range of 100 to 120º/s -- to achieve a uniform stimulus for all subjects. For both, the mean gain was 1.08 ± 0.10 SD. Thus, it appears that a small variation in stimulus does not adversely affect results in healthy subjects. If we normalize the gain for the target distance (140 cm, in our study), we obtain a mean gain of 1.02 (normal range 0.84-1.20, mean ± 2 SD), which is even closer to the ideal of unity.

Lasker et al. (2002) reported a significant increase in AVOR gain in response to high-velocity head rotations during near-target viewing (15 cm) compared with far-target viewing (124 cm), as a result of vergence-mediated modulation of the reflex. Their mean gains were 1.25 ± 0.08 SD versus 1.01 ± 0.06 SD. Crane and

Demer (1998) found also horizontal AVOR gain to increase with near targets. In our study, eight subjects underwent testing with both target distances: 140 and 15 cm, and our results were consistent the earlier ones.

Patients with unilateral vestibular schwannoma

Of our 38 patients, 45% had normal gain on both sides preoperatively. After surgery, all patients had abnormal gain on the ipsilateral side, and in almost half of them the gain was significantly decreased on the contralateral side, as well. Before surgery, impulses toward the side of VS evoked an AVOR with clearly lower gain than did those towards the intact side (0.83 versus 0.98). After tumor removal, this difference was even more profound (0.53 versus 0.87). These asymmetries are based on primary afferent physiology. An excitatory stimulus may raise the firing rate of a vestibular neuron from < 100 spikes/s to several hundred, but an inhibitory stimulus can drive firing only up to the inhibitory cut-off of 0 spikes/s. The input for eyes to move during ipsilateral head movements after a total unilateral vestibular lesion comes from the contralateral side, and eye velocities of 50 to 75º/s measured in our study are in agreement with those of Cremer et al. (1998).

The postoperative mean gain of approximately 0.5 on the ipsilateral side and 0.85 on the contralateral side was higher than the usually reported 0.2 to 0.4 and 0.55 to 0.85, measured with a quantitative head impulse test after unilateral vestibular deafferentation (Aw et al. 1996a, Carey et al. 2002, Cremer et al. 1998, Halmagyi et al. 1990). The explanation is that the gain is dependent on stimulation intensity. Because we analyzed the gain in a head velocity range of 100 to 120º/s to normalize the stimulus between every patient, the residual eye velocities of 50 to 75º/s compared to these head velocities will provide a gain of this magnitude. Our analysis window was 120 milliseconds, during which the mean velocity of 170º/s was achieved. Our head velocity range used for analysis corresponds to a time-interval approximately of 70 to 85 milliseconds after the beginning of the head movement. This may have allowed some early refixation saccades to be included, as they may occur as early as 70 milliseconds after the beginning of the head impulse (Weber et al. 2008). However, since most of the saccades occur later, their effect on gain seems to be negligible. Later, we have taken account of this by making our current impulses shorter, to peak at 100 milliseconds, and faster, not to lose in velocity.

These studies with lower gain have used head velocities as high as 300º/s and acceleration up to 4 000º/s², which indeed enable a more profound decrease in gain. Crane and Demer (1998) have demonstrated that when higher accelerations were applied, the AVOR gain decreased. Similarly, gain decrease was more profound with accelerations up to 6 000º/s² than with low accelerations at 750º/s² (Black et al. 2005, Weber et al. 2008). However, an increase in acceleration

usually accompanies higher velocities, and velocities ≥ 200º/s have produced more variable results than have velocities < 200º/s (Roy and Tomlinson 2004). This could result from many causes, but decoupling of the velocity sensors and especially an increase in noise levels are the most probable.

Asymmetry in gain

In the literature, the normative range for directional asymmetry in gain (mean ± 2 SD) ranges from 8 to 13% (Allison et al. 1997, Park et al. 2005, Weber et al. 2008). The mean asymmetry in gain of 3.7 ± 2.8% SD in our work agrees well with the normal values from other studies. Our normative range (mean ± 2 SD) for asymmetry remained within 10%, significantly narrower than the wide normal range of ± 25 to 30% for unilateral weakness in the caloric test. This fact makes it a promising variable for detection of side difference in patients with unilateral vestibular pathology.

Half the patients had abnormal asymmetry in gain preoperatively. After tumor removal, the asymmetry in gain was pathologic in all patients. Using helmet-induced head impulses, Tabak et al. (1997b) noticed abnormal asymmetry in 80% of their postoperative patients. This difference may be due to patient characteristics, but probably the lower stimulation intensity of < 100º/s has worsened their sensitivity to detect asymmetry. Instead, their mean asymmetry in gain of 20 to 24% after VS removal is in agreement with the 25% in our study.

Latency

Mean delay between head movement and compensatory eye movement in healthy controls was 3.4 ± 6.3 milliseconds. This value is smaller than but comparable to the latency measured with passive head-on-body rotation by Aw et al. (1996b) (mean 7.5 ± 2.9 milliseconds SD) and by Della Santina et al. (2002) (mean 11.0 ± 3.3 milliseconds SD), and is comparable to the whole-body rotations reported by Crane and Demer (1998) (5-10 milliseconds). Furthermore, our value is consistent with the latency reported with the helmet technique (5-9 milliseconds) (Collewijn and Smeets 2000, Tabak et al. 1997a).

Reliable calculation of latency cannot allow any slippage of head or eye during the measurement. Minor et al. (1999) attached the search coils rigidly to the skulls of squirrel monkeys and obtained a latency of 7.3 ± 1.5 milliseconds SD, which is comparable to latency in humans. Helmet slippage should amplify latency and consequently reduce gain in our test. Significant slippage of the helmet during our test seemed unlikely, because our latency was shorter than

reported, and the mean gain was 2% greater than the ideal. Furthermore, our single test with another head movement sensor rigidly attached to the skull failed to reveal any significant decoupling between head and helmet. The magnetic search coil technique should be advantageous for latency registration, although Aw et al. (1996b) emphasized the importance of tight fixation of the head and eye coils during the measurements with high acceleration to prevent bias.

The relatively wide range of our latency values could be in part explained by the electro-oculography recording technique, which is more vulnerable to noise than are other techniques. Filtering may have slightly straightened the eye movement curve, which may have shifted the crossing of the eye velocity threshold earlier. Use of a velocity threshold to detect the beginning of eye and head movement is common (Aw et al. 1996a, Carey et al. 2002, Della Santina et al. 2002, Weber et al. 2008). This induces a source of error for latency calculation, since a low gain in patients always leads to an increase in latency. However, the alternative method of calculating latency, using linear regression over certain velocities and extrapolating the starting point, has produced similar results: abnormal mean ± SD (20.7 ± 8.6 milliseconds) values overlapping a wide normal range up to 18 milliseconds (Collewijn and Smeets 2000, Tabak et al. 1997b). For example, in our study, of 38 VS patients measured preoperatively, only two had a latency abnormality independent of gain or asymmetry abnormality. In sum, latency seems to be a less useful parameter than the gain and asymmetry calculation in clinical evaluation of horizontal AVOR.

Miscellaneous

No correlation appeared pre- and postoperatively with subjective balance disturbance and quantitative measurements of vestibular function. This lack of correlation indicates that the altered peripheral input alone is not principally responsible for the handicap, a fact also evident in our previous study with VFP. Nor could the postoperative vestibular disability be predicted based on preoperative AVOR performance during motion stimuli, nor in the caloric test. Therefore, peripheral vestibular testing cannot be recommended as a routine follow-up measure after the surgery.

Our motorized head impulse rotator, as well as the caloric test, mainly evaluates the horizontal SCC. These tests examine a different dynamic range: the former evaluates the low-frequency range, and the latter, higher frequencies used during natural locomotion (Halmagyi et al. 2001, Schmid-Priscoveanu et al. 2001). There emerged in our work a highly significant correlation between unilateral weakness in the caloric test and asymmetry in gain, which indicates that VS deteriorates both low and high frequencies of the AVOR simultaneously. Tumors located in the inferior part of the vestibular nerve or which arise from the superior part and are not sufficiently disturbing nerve function, will go

undetected. Indeed, in our patients with VS, preoperative caloric responses were symmetrical for 41%. Similarly, normal responses to high-frequency motion stimuli were common (24%). These findings suggest that a substantial proportion of patients with VS may have partially or totally preserved vestibular function preoperatively, and thus screening of VS should not be based on findings from these tests alone.

Hearing loss seems to be the most annoying symptom before surgery, as reflected by its impact on quality of life. Postoperatively, dizziness was regarded as more important. This finding indicates that the patients are able to adapt to their unilateral hearing disability, but unilateral profound loss of vestibular function significantly impacts their everyday life for at least some months after surgery.

6.3 FUTURE ASPECTS

Based on our results with VFP, this method is not a diagnostic tool for patients with balance disorders. This is true for all present posturography techniques in general, but future developments may improve the situation. The VFP is valuable as quantitative measure of postural control and can be utilized as a follow-up tool in individual patients with vestibular disorders.

The present study with motorized head impulses handled measurement of horizontal AVOR in patients with VS and showed reliable results in detecting unilateral vestibular loss. Measurements with the MHIT of a limited group of patients with bilateral vestibular deficits have demonstrated a deep gain deficit on both sides; one example of this was reported in Study IV. To date, the MHIT has been used for 35 patients with vestibular neuritis, for 20 patients before and after cochlear implantation, for 10 patients with Ménière disease, for 8 patients with bilateral vestibular deficit, and on about 60 patients who were dizzy without any definite diagnosis. The data have already been utilized in daily clinical practice, and scientific analyses in future will reveal more details as to the strength and clinical utility of this MHIT in other patient populations.

7. CONCLUSIONS

1. The repeatability of VFP in individual patients was good, although the slight learning effect seen in two of the four VFP parameters in healthy volunteers has to be taken into account when evaluating postural control serially with VFP. The VFP is an objective method to assess and follow up active postural control within individual subjects.

2. Postural control in patients with VS was disturbed, as assessed with VFP, although this disturbance was not severe even one month after surgery. The preoperative postural inaccuracy persisted in most patients also postoperatively. This abnormality in VFP may be interpreted as an indication for more aggressive rehabilitation. Side difference in postural control was rare. In contrast to unilateral weakness in the caloric test, the VFP seems to take into account more than only the peripheral vestibular system in the evaluation of functional postural control.

3. The horizontal AVOR measurements with MHIT were performed in healthy volunteers. Normal ranges for gain, asymmetry in gain, and latency for MHIT were established, ones comparable to those reported from other techniques with head impulse stimuli. This suggests that the MHIT allows reliable and safe measurement of the AVOR, and this method is a useful tool in clinical assessment of the AVOR.

4. Preoperatively, the horizontal AVOR, measured with MHIT, was preserved on the ipsilateral side in about one-quarter of the patients, whereas it remained abnormal in every patient about 4 months after surgery. The decreased gain and increased asymmetry seen postoperatively is in agreement with published data, from works using head impulses, bearing in mind our stimulus intensity. Vestibular disability could not be predicted based on AVOR performance either during motion stimuli, or in the caloric test. The non-invasive MHIT allows fast and relevant evaluation of peripheral vestibular pathology, as demonstrated among patients with unilateral VS.

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